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(54) Title: VARIANTS OF ALTERNATIVE SPLICING

(57) Abstract: The present invention concerns novel variants, amino acid and nucleic acid sequences obtained by alternative splicing of known sequences, expression vectors and host cells containing the variants' nucleic acid sequence, and antibodies reactive with the variants' products. The invention also concerns pharmaceutical compositions containing any of the above as well as methods of detection. A preferred example is the angiotensin converting enzyme (ACE) variant.

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## VARIANTS OF ALTERNATIVE SPLICING

### FIELD OF THE INVENTION

The present invention concerns novel nucleic acid sequences, vectors and host cells containing them, amino acid sequences encoded by said sequences, and antibodies reactive with said amino acid sequences, as well as pharmaceutical compositions comprising any of the above. The present invention further concerns methods for screening for candidate activators or deactivators utilizing said amino acid sequences.

### BACKGROUND OF THE INVENTION

Alternative splicing (AS) is an important regulatory mechanism in higher eukaryotes (P.A. Sharp, *Cell* 77, 805-8152 (1994)). It is thought to be one of the most important mechanisms for differential expression related to tissue or development stage specificity. It is known to play a major role in numerous biological systems, including human antibody responses, and sex determination in *Drosophila*, (S. Stamm, M.Q. Zhang, T.G. Marr and D.M. Helfman, *Nucleic Acids Research* 22, 1515-1526 (1994); B. Chabot, *Trends Genet.* 12, 472-478 (1996); R.E. Breitbart, A. Andreadis, B. Nadal-Ginard, *Annual Rev. Biochem.*, 56, 467-495 (1987); C.W. Smith, J.G. Patton, B. Nadal-Ginard, *Annu. Rev. Genet.*, 27, 527-577 (1989)).

Until recently it was commonly believed that alternative splicing existed in only a small fraction of genes (about 5%). A recent observation based on literature survey of known genes revises this conservative estimate to as high as an estimate that at least 30% of human genes are alternatively spliced (M.S. Gelfand, I. Dubchak, I. Draluk and M. Zorn, *Nucleic Acids Research* 27, 301-302 (1999)). The importance of the actual frequency of this phenomenon lies not only



in the direct impact on the number of proteins created (100,000 human genes, for example, would be translated to a much higher number of proteins), but also in the diversity of functionality derived from the process.

Several mechanisms at different stages may be held responsible for the complexity of higher eukaryote which include: alternative splicing at the transcription level, RNA editing at the post-transcriptional level, and post-translational modifications are the ones characterized to date.

Angiotensin I-converting enzyme (ACE) is a peptidyl dipeptide hydrolase that is located mainly on the luminal surface of vascular endothelial cells but also in cells derived from the monocyte-macrophage system. Physiologically, ACE is a key enzyme in the renin-angiotensin system, converting angiotensin I into the potent vasopressor angiotensin II and also inactivating the vasodilator bradykinin.

Increased serum ACE activity (SACE) has been reported in pathologies involving stimulation of the monocytic cell line, primarily granulomatous diseases. Sarcoidosis is the most frequent and the better studied of these diseases; high SACE is not only a well-established marker for the diagnosis but is also a useful tool for following its course and evaluating the effect of therapy of this disease.

SACE can also be increased in nonsarcoidotic pulmonary granulomatous diseases such as silicosis and asbestosis, in extrathoracic granulomatous pathologies such as Gauchers disease and leprosis, and, to a lesser extent, in nongranulomatous disorders such as hyperthyroidism or cholestasis.

Decreased SACE has been reported in vascular pathologies involving an endothelial abnormality, such as deep vein thrombosis, and in endothelium dysfunctions related to the toxicity of chemo- and radiotherapy used in cancers, leukemias, and hematopoietic or organ transplantations.

SACE is also of interest for monitoring arterial hypertension treated with specific synthetic ACE inhibitors.

Various methods have been developed for determining SACE activities. The most widely used is the spectrophotometric assay using hippuryl-histidyl-leucine as substrate. Fluorimetric and radiochemical assays using both classic and novel substrates have been proposed, but they are time consuming, require special apparatus, and are not suited to automation. Kinetic spectrophotometry of furylacryloyl-phenylalanyl-glycyl-glycine hydrolysis is now used extensively because it is easy to automatize.

Information obtained in the last decade indicates that angiotensin II increases the production of several autocrine factors, including transforming growth factor beta1 (TGF-beta1), tumor necrosis factor-alpha (TNF-alpha), and platelet-derived growth factor A chain (PDGF). Angiotensin also increases the release of other growth factors such as endothelin, platelet-activating factor (PAF), and interleukin 6. In addition, it increases the "activity" of nuclear factor-kappaB (NF-kappaB) and the synthesis of angiotensinogen. The emerging picture indicates that the actions of angiotensin II may be related to factors that are released or upregulated by angiotensin II, possibly through NF-kappaB.

## GLOSSARY

In the following description and claims use will be made, at times, with a variety of terms, and the meaning of such terms as they should be construed in accordance with the invention is as follows:

***"Variant nucleic acid sequence"*** – the sequence shown in any one of SEQ ID NO: 1 to SEQ ID NO: 87, native and known genes. It should be emphasized that the novel variants of the present invention are naturally occurring sequences resulting from alternative splicing of genes and not merely truncated, mutated or fragmented forms of known sequences which are artificially produced.

**"Angiotensin converting enzyme variant (ACEV)"** - a sequence shown in SEQ ID NO: 57 or 85 sequences having at least 90% identity (see below) to said sequence and *fragments* (see below) of the above sequences of least 20 b.p. long. These sequences are sequences coding for a novel, naturally occurring, alternative splice variants of the mouse angiotensin converting enzyme which convert angiotensin I to angiotensin II by release of the terminal His-Leu resulting in increase of vasoconstrictor activity of angiotensin.

**"Variant product - also referred at times as the "variant protein" or "variant polypeptide"** - is an amino acid sequence encoded by the variant nucleic acid sequence SEQ ID NO: 88 to SEQ ID NO: 174.

**"ACEV product or ACEV protein"** - amino acid coded by the ACEV nucleic acid which is a naturally occurring mRNA sequence obtained as a result of alternative splicing of the ACE gene. The amino acid sequence may be a peptide, a protein, as well as peptides or proteins having *chemically modified* amino acids (see below) such as a glycopeptide or glycoprotein. The variant products are shown in SEQ ID NO: 144 or 172. The term also includes *homologies* (see below) of said sequences in which one or more amino acids has been added, deleted, *substituted* (see below) or *chemically modified* (see below) as well as *fragments* (see below) of this sequence having at least 10 amino acids. The above two products may be secreted.

**"Nucleic acid sequence"** - a sequence composed of DNA nucleotides, RNA nucleotides or a combination of both types and may include natural nucleotides, chemically modified nucleotides and synthetic nucleotides.

**"Amino acid sequence"** - a sequence composed of any one of the 20 naturally appearing amino acids, amino acids which have been *chemically modified* (see below), or composed of synthetic amino acids.

**"Fragment of variant nucleic acid sequence"** and **"fragment of ACEV nucleic acid sequence"** - novel short stretch of nucleic acid sequences of at least 20 b.p., which does not appear as a continuous stretch in the *original nucleic acid sequence* (see below). The fragment may be a sequence which was previously  
5 undescribed in the context of the published RNA and which affects the amino acid sequence encoded by the known gene. For example, where the variant nucleic includes a sequence which was not included in the original sequence (for example a sequence which was an intron in the original sequence) the fragment may contain said additional sequence. The fragment may also be a region which  
10 is not an intron, which was not present in the original sequence. For example where the variant lacks a non-terminal region which was present in the original sequence. The two stretches of nucleotides spanning this region (upstream and downstream) are brought together by splicing in the variant, but are spaced from each by the spliced out region in the original sequence and are thus not  
15 continuous in the original sequence. A continuous stretch of nucleic acids comprising said two splicing stretches of nucleotides is not present in the original sequence and thus falls under the definition of fragment.

**"Fragments of variant products"** - novel amino acid sequences coded by the  
20 **"fragment of variant nucleic acid sequence"** or **"fragment of ACEV nucleic acid sequence"** defined above.

**"Homologues of variants"** - amino acid sequences of variants in which one or more amino acids has been added, deleted or replaced. The addition, deletion or  
25 replacement should be in the regions or adjacent to regions where the variant differs from the *original sequence* (see below).

**"Conservative substitution"** - refers to the substitution of an amino acid in one class by an amino acid of the same class, where a class is defined by common  
30 physicochemical amino acid side chain properties and high substitution

frequencies in homologous proteins found in nature, as determined, for example, by a standard Dayhoff frequency exchange matrix or BLOSUM matrix. [Six general classes of amino acid side chains have been categorized and include: Class I (Cys); Class II (Ser, Thr, Pro, Ala, Gly); Class III (Asn, Asp, Gln, Glu);  
5 Class IV (His, Arg, Lys); Class V (Ile, Leu, Val, Met); and Class VI (Phe, Tyr, Trp). For example, substitution of an Asp for another class III residue such as Asn, Gln, or Glu, is a conservative substitution.

**"Non-conservative substitution"** - refers to the substitution of an amino acid in  
10 one class with an amino acid from another class; for example, substitution of an Ala, a class II residue, with a class III residue such as Asp, Asn, Glu, or Gln.

**"Chemically modified"** - when referring to the product of the invention, means a product (protein) where at least one of its amino acid residues is modified either by  
15 natural processes, such as processing or other post-translational modifications, or by chemical modification techniques which are well known in the art. Among the numerous known modifications typical, but not exclusive examples include: acetylation, acylation, amidation, ADP-ribosylation, glycosylation, GPI anchor formation, covalent attachment of a lipid or lipid derivative, methylation,  
20 myristylation, pegylation, prenylation, phosphorylation, ubiquitination, or any similar process.

**"Biologically active"** - refers to the variant product having some sort of biological activity, for example, some physiologically measurable effect on target  
25 cells, molecules or tissues.

**"Immunologically active"** defines the capability of a natural, recombinant or synthetic variant product, or any fragment thereof, to induce a specific immune response in appropriate animals or cells and to bind with specific antibodies.  
30 Thus, for example, an immunologically active fragment of variant product

denotes a fragment which retains some or all of the immunological properties of the variant product, e.g. can bind specific anti-variant product antibodies or which can elicit an immune response which will generate such antibodies or cause proliferation of specific immune cells which produce variant.

5

**"Optimal alignment"** - is defined as an alignment giving the highest percent identity score. Such alignment can be performed using a variety of commercially available sequence analysis programs, such as the local alignment program LALIGN using a ktup of 1, default parameters and the default PAM. A preferred  
10 alignment is the one performed using the CLUSTAL-W program from MacVector (TM), operated with an open gap penalty of 10.0, an extended gap penalty of 0.1, and a BLOSUM similarity matrix. If a gap needs to be inserted into a first sequence to optimally align it with a second sequence, the percent identity is calculated using only the residues that are paired with a corresponding  
15 amino acid residue (i.e., the calculation does not consider residues in the second sequences that are in the "gap" of the first sequence). In case of alignments of known gene sequences with that of the new variant, the optimal alignment invariably included aligning the identical parts of both sequences together, then keeping apart and unaligned the sections of the sequences that differ one from the  
20 other.

**"Having at least 90% identity"** - with respect to two amino acid or nucleic acid sequence sequences, refers to the percentage of residues that are identical in the two sequences when the sequences are optimally aligned. Thus, 90% amino acid  
25 sequence identity means that 90% of the amino acids in two or more optimally aligned polypeptide sequences are identical, however this definition explicitly excludes sequences which are 100% identical with the original sequence from which the variant of the invention was varied.

**"Isolated nucleic acid molecule having an variant nucleic acid sequence"** - is a nucleic acid molecule that includes the coding variant nucleic acid sequence. Said isolated nucleic acid molecule may include the variant nucleic acid sequence as an independent insert; may include the variant nucleic acid sequence fused to an additional coding sequences, encoding together a fusion protein in which the variant coding sequence is the dominant coding sequence (for example, the additional coding sequence may code for a signal peptide); the variant nucleic acid sequence may be in combination with non-coding sequences, e.g., introns or control elements, such as promoter and terminator elements or 5' and/or 3' untranslated regions, effective for expression of the coding sequence in a suitable host; or may be a vector in which the variant protein coding sequence is a heterologous.

**"Expression vector"** - refers to vectors that have the ability to incorporate and express heterologous DNA fragments in a foreign cell. Many prokaryotic and eukaryotic expression vectors are known and/or commercially available. Selection of appropriate expression vectors is within the knowledge of those having skill in the art.

**"Deletion"** - is a change in either nucleotide or amino acid sequence in which one or more nucleotides or amino acid residues, respectively, are absent.

**"Insertion" or "addition"** - is that change in a nucleotide or amino acid sequence which has resulted in the addition of one or more nucleotides or amino acid residues, respectively, as compared to the naturally occurring sequence.

**"Substitution"** - replacement of one or more nucleotides or amino acids by different nucleotides or amino acids, respectively. As regards amino acid sequences the substitution may be conservative or non- conservative.

**"Antibody"** – refers to IgG, IgM, IgD, IgA, or IgG antibody. The definition includes polyclonal antibodies or monoclonal antibodies. This term refers to whole antibodies or fragments of the antibodies comprising the antigen-binding domain of the anti-variant product antibodies, e.g. antibodies without the Fc portion, single chain antibodies, fragments consisting of essentially only the variable, antigen-binding domain of the antibody, etc.

***Distinguishing antibody*** – an antibody capable of binding to the variant product and not the original amino acid sequence from which it has been varied, or an antibody capable of binding to the original nucleic acid sequence and not to the variant production.

**"Activator"** - as used herein, refers to a molecule which mimics the effect of the natural variant product or at times even increases or prolongs the duration of the biological activity of said product, as compared to that induced by the natural product. The mechanism may be by any mechanism known to prolonging activities of biological molecules such as binding to receptors; prolonging the lifetime of the molecules; increasing the activity of the molecules on its target; increasing the affinity of molecules to its receptor; inhibiting degradation or proteolysis of the molecules, or mimicking the biological activity of the variants on their targets, etc. Activators may be polypeptides, nucleic acids, carbohydrates, lipids, or derivatives thereof, or any other molecules which can bind to and activate the variant product.

**"Deactivator" or ("Inhibitor")** - refers to a molecule which modulates the activity of the variant product in an opposite manner to that of the activator, by decreasing or shortening the duration of the biological activity of the variant product. This may be done by any mechanism known to deactivate or inhibit biological molecules such as block of the receptor, block of active site, competition on binding site in target, enhancement of degradation, etc.



Deactivators may be polypeptides, nucleic acids, carbohydrates, lipids, or derivatives thereof, or any other molecules which bind to and modulate the activity of said product.

- 5 *"Treating a disease"* - refers to administering a therapeutic substance effective to ameliorate symptoms associated with a disease, to lessen the severity or cure the disease, or to prevent the disease from occurring.

*"Detection"* - refers to a method of detection of a disease, disorder, pathological  
10 or normal condition. This term may refer to detection of a predisposition to a disease as well as for establishing the prognosis of the patient by determining the severity of the disease.

*"Probe"* - the variant nucleic acid sequence, or a sequence complementary  
15 therewith, when used to detect presence of other similar sequences in a sample. The detection is carried out by identification of hybridization complexes between the probe and the assayed sequence. The probe may be attached to a solid support or to a detectable label.

20 *"Original sequence"* - the amino acid or nucleic acid sequence from which the variant of the invention have been varied as a result of alternative slicing.

## SUMMARY OF THE INVENTION

The present invention is based on the finding of several novel, naturally occurring splice variants, which are naturally occurring sequences obtained by  
25 alternative splicing of known genes. The novel splice variants of the invention are not merely truncated forms, fragments or mutations of known genes, but rather novel sequences which naturally occur within the body of individuals.

In particular the present invention concerns variants of alternative splice variants of angiotensin converting enzyme (ACEV).

The term "*alternative splicing*" in the context of the present invention and claims refers to: intron inclusion, exon exclusion, addition or deletion of terminal sequences in the variant as compared to the original sequences, as well as to the possibility of "*intron retention*". Intron retention is an intermediate stage in the  
5 processing of RNA transcripts, where prior to production of fully processed mRNA the intron (naturally spliced in the original sequence) is retained in the variant. These intermediately processed RNAs may have physiological significance and are also within the scope of the invention.

The novel variant products of the invention, including the ACEV-variant  
10 (ACEV), may have the same physiological activity as the original peptide from which they have been varied (although perhaps at a different level); may have an opposite physiological activity from the activity featured by the original peptide from which they are varied; may have a completely different, unrelated activity to the activity of the original from which they are varied; or alternatively may have no  
15 activity at all and this may lead to various diseases or pathological conditions. The novel variants of the invention may differ from the original sequence, from which they were varied by alternative splicing, by physiological properties not relating directly to their activities such as: tissue localization, temporal pattern of expression, rate of clearance, rate of degradation, manner of up- or down  
20 regulation, association with co-factors and cellular elements etc.

The novel variants may also serve for detection purposes, i.e. their presence or level may be indicative of a disease, disorder, pathological or normal condition or alternatively the ratio between the level variants and the level original peptide from which they were varied, or the ratio to other variants may be indicative to a  
25 disease, disorder, pathological or normal condition.

For example, for detectional purposes, it is possible to establish differential expression of various variants in various tissues. A certain variant may be expressed mainly in one tissue, while the original sequence from which it has been varied, or another variant may, be expressed mainly in another tissue.  
30 Understanding of the distribution of the variants in various tissues may be helpful

in basic research, for understanding the physiological function of the genes as well as may help in targeting pharmaceuticals or developing pharmaceuticals.

The study of the variants may also be helpful to distinguish various stages in the life cycles of the same type of cells which may also be helpful for development  
5 of pharmaceuticals for various pathological conditions in which cell cycles is non-normal, notably cancer.

Detection of various diseases in accordance with the invention is especially useful for detection of diseases which are associated with the function, (over function, under function, or malfunction) of proteins of the original sequence from  
10 which each variant of the invention has been obtained by alternative splicing. A list of the original proteins are given in the "Detailed Description" part of the specification. Thus, for example, if variant of SEQ ID NO: 3 is obtained from an original sequence which is coagulation factor XII, this sequence may be used to detect diseases involving excessive or diminished blood coagulation.

15 Thus the detection may be by determination of the presence or the level of expression of the variant within a specific cell population, comprising said presence or level between various cell types in a tissue, between different tissues and between individuals.

Where the variant in the angiotensin converting enzyme (ACEV) the  
20 detection may be used for detection (including disposition) of one of the following diseases.

Cardiovascular diseases:

Including hypertension, neurological damage due to cerebral  
circulatory disorders, peripheral vascular diseases, arteriosclerosis, heart and kidney  
25 diseases relating to blood pressure, erection problems and migraine problems relating to circulation functions, heart failures (including recurrent infraction in patients with left ventricular dysfunction), acute phase of myocardial infarction, coronary arterial thrombosis and cardiac insufficiency.

Renal diseases:

Hypertension adrenal injury (particularly in patients with type I or II diabetes), diabetic nephropathy, renal function deterioration in glomerular diseases

Muscular diseases:

5 Diseases involving growth of smooth muscle cells such as hypertrophy.

Immune disorders:

Various autoimmune diseases and diseases involving inflammatory mechanisms, for example, autoimmune manifestation affects in sarcoidosis, generation of immune complex nephritis, autoimmune encephatomyelitis, marker  
10 for chronic fatigue-immune dysfunction syndrome.

Multiple sclerosis:Cancer:

Especially those cancers effected by different growth factors including endothelia, platelet-activating factor (PAF) and interleukin 6. Examples of such  
15 cancers are tumors of the vascular system, and leukemias.

Diabetes:

Sarcoidosis – a disease of unknown origin characterized by the formation of granulomatous lesions that appear especially in the liver, lungs, skin and lymph nodes.

20 Nonaroidotic Pulmonary Granulomatous Diseases:

Such as silicosis and asbestosis, in extrathoracic granulomatous pathologies such as Gauchers disease and leprosis, and, to a lesser extent, in nongranulomatous disorders such as hyperthyroidism or cholestasis. (increased sACE)

25 Vascular Pathologies Involving An Endothelial Abnormality:

Deep vein thrombosis, and in endothelium dysfunctions related to the toxicity of chemo- and radiotherapy used in cancers, leukemias, and hematopoietic or organ transplantations.

Thus the present invention provides by its first aspect, a novel isolated  
30 nucleic acid molecule comprising or consisting of any one of the coding sequence

SEQ ID NO: 1 to SEQ ID NO: 87, fragments of said coding sequence having at least 20 nucleic acids (provided that said fragments are continuous stretches of nucleotides not present in the original sequence from which the variant was varied), or a molecule comprising a sequence having at least 90% identity to SEQ ID  
5 NO: 1 to SEQ ID NO: 87, provided that the molecule is not completely identical to the original sequence from which the variant was varied. In particular, the above variant is that of SEQ ID NO: 57 or SEQ ID NO: 85 being the ACEV nucleic acid sequence.

The present invention further provides a protein or polypeptide comprising  
10 or consisting of an amino acid sequence encoded by any of the above nucleic acid sequences, termed herein "*variant product*", for example, an amino acid sequence having the sequence as depicted in any one of SEQ ID NO: 88 to SEQ ID NO: 174, fragments of the above amino acid sequence having a length of at least 10 amino acids coded by the above fragments of the nucleic acid sequences, as well as  
15 homologues of the above amino acid sequences in which one or more of the amino acid residues has been substituted (by conservative or non-conservative substitution) added, deleted, or chemically modified. In particular, the product is the amino acid sequence of the ACEV as depicted in SEQ ID NO: 144 or 172.

The deletions, insertions and modifications should be in regions, or adjacent  
20 to regions, wherein the variant differs from the original sequence.

For example, where the variant is different from the original sequence by addition of a short stretch of 10 amino acids, in the terminal or non-terminal portion of the peptide, the invention also concerns homologues of that variant where the additional short stretch is altered for example, it includes only 8  
25 additional amino acids, includes 13 additional amino acids, or it includes 10 additional amino acids, however some of them being conservative or non-conservative substitutes of the original additional 10 amino acids of the novel variants. In all cases the changes in the homolog, as compared to the original sequence, are in the same regions where the variant differs from the original  
30 sequence, or in regions adjacent to said region.

Another example is where the variant lacks a non-terminal region (for example of 20 amino acids) which is present in the original sequence (due for example to exon exclusion). The homologues may lack in the same region only 17 amino acids or 23 amino acids. Again the deletion is in the same region where the  
5 variant lacks a sequence as compared to the original sequence, or in a region adjacent thereto.

It should be appreciated that once a man versed in the art's attention is directed to the importance of a specific region, due to the fact that this region differs in the variant as compared to the original sequence, there is no problem in  
10 derivating said specific region by addition to it, deleting from it, or substituting some amino acids in it. Thus homologues of variants which are derivated from the variant by changes (deletion, addition, substitution) only in said region as well as in regions adjacent to it are also a part of the present invention. Generally, if the variant is distinguished from the original sequence by some sort of physiological  
15 activity, then the homolog is distinguished from the original sequence in essentially the same manner.

The present invention further provides nucleic acid molecule comprising or consisting of a sequence which encodes the above amino acid sequences, (including the fragments and homologues of the amino acid sequences and in  
20 particular the ACEV amino acid sequence). Due to the degenerative nature of the genetic code, a plurality of alternative nucleic acid, beyond those depicted in any one of SEQ ID NO: 1 to SEQ ID NO: 87, can code for the amino acid sequence of the invention. Those alternative nucleic acid sequences which code for the same amino acid sequences codes by the sequence SEQ ID NO: 1 to SEQ ID NO: 87 are  
25 also an aspect of the of the present invention.

The present invention further provides expression vectors and cloning vectors comprising any of the above nucleic acid sequences, as well as host cells transfected by said vectors.

The present invention still further provides pharmaceutical compositions comprising, as an active ingredient, said nucleic acid molecules, said expression vectors, or said protein or polypeptide.

These pharmaceutical compositions are suitable for the treatment of diseases  
5 and pathological conditions, which can be ameliorated or cured by raising the level of any one of the variant products of the invention. In particular, those diseases are diseases which are associated with malfunction or under function of the original sequence (for example, given in the "Detailed Description" part of the specification). Thus for example, SEQ ID NO: 3 and sequences encoded thereby  
10 may be used to treat diseases associated with coagulation of blood.

By a second aspect, the present invention provides a nucleic acid molecule comprising or consisting of a non-coding sequence which is complementary to that of any one of SEQ ID NO: 1 to SEQ ID NO: 87, or complementary to a sequence having at least 90% identity to said sequence (with the proviso added above) or a  
15 fragment of said two sequences (according to the above definition of fragment). The complementary sequence may be a DNA sequence which hybridizes with any one of SEQ of ID NO: 1 to SEQ ID NO: 87 or hybridizes to a portion of that sequence having a length sufficient to inhibit the transcription of the complementary sequence. The complementary sequence may be a DNA sequence  
20 which can be transcribed into an mRNA being an antisense to the mRNA transcribed from any one of SEQ ID NO: 1 to SEQ ID NO: 87 or into an mRNA which is an antisense to a fragment of the mRNA transcribed from any one of SEQ ID NO: 1 to SEQ ID NO: 87 which has a length sufficient to hybridize with the mRNA transcribed from SEQ ID NO: 1 to SEQ ID NO: 87, so as to inhibit its  
25 translation. The complementary sequence may also be the mRNA or the fragment of the mRNA itself.

The nucleic acids of the second aspect of the invention may be used for therapeutic or diagnostic applications for example as probes used for the detection of the variants of the invention. The presence of the variant transcript or the level of  
30 the variant transcript may be indicative of a multitude of diseases, disorders and

various pathological as well as normal conditions for example, as indicated above for the variants in general, and for the ACEV in particular. In addition or alternatively, the ratio of the level of the transcripts of the variants of the invention may also be compared to that of the transcripts of the original sequences from which have been varied, or to the level of transcript of other variants, and said ratio may be indicative to a multitude of diseases, disorders and various pathological and normal conditions.

The present invention also provides expression vectors comprising any one of the above defined complementary nucleic acid sequences and host cells transfected with said nucleic acid sequences or vectors, being complementary to those specified in the first aspect of the invention.

The invention also provides anti-variant product antibodies, namely antibodies directed against the variant product which specifically bind to said variant product. Said antibodies are useful both for diagnostic and therapeutic purposes. For example said antibody may be as an active ingredient in a pharmaceutical composition as will be explained below.

The present invention also provides pharmaceutical compositions comprising, as an active ingredient, the nucleic acid molecules which comprise or consist of said complementary sequences, or of a vector comprising said complementary sequences. The pharmaceutical composition thus provides pharmaceutical compositions comprising, as an active ingredient, said anti-variant product antibodies.

The pharmaceutical compositions comprising said anti-variant product antibodies or the nucleic acid molecule comprising said complementary sequence, are suitable for the treatment of diseases and pathological conditions where a therapeutically beneficial effect may be achieved by neutralizing the variant (either at the transcript or product level) or decreasing the amount of the variant product or blocking its binding to its target, for example, by the neutralizing effect of the antibodies, or by the effect of the antisense mRNA in decreasing the expression level of the variant sequence.



Examples of diseases which can be treated either with ACEV sequence, an expression vector comprising that sequence, a sequence complementary to the ACEV sequence, an expression vector comprising said complementary sequence, ACEV product or an antibody to the product is any one of the diseases mentioned  
5 in connection with the detection aspect above.

According to the third aspect of the invention the present invention provides methods for detecting the level of the transcript (mRNA) of said variant product in a body fluid sample, or in a specific tissue sample, for example by use of probes comprising or consisting of said coding sequences; as well as methods for detecting  
10 levels of expression of said product in tissue, e.g. by the use of antibodies capable of specifically reacting with the variant products of the invention. Detection of the level of the expression of the variant of the invention in particular as compared to that of the original sequence from which it was varied or compared to other variant sequences all varied from the same original sequence may be indicative of a  
15 plurality of physiological or pathological conditions. A preferred example is the detection of ACEV nucleic acid sequence, ACEV product or anti-ACEV antibody.

The method, according to this latter aspect, for detection of a nucleic acid sequence which encodes the variant product in a biological sample, comprises the steps of:

- 20 (a) providing a probe comprising at least one of the nucleic acid sequences defined above;
- (b) contacting the biological sample with said probe under conditions allowing hybridization of nucleic acid sequences thereby enabling formation of hybridization complexes;
- 25 (c) detecting hybridization complexes, wherein the presence of the complexes indicates the presence of nucleic acid sequence encoding the variant product in the biological sample.

The method as described above is qualitative, i.e. indicates whether the transcript is present in or absent from the sample. The method can also be  
30 quantitative, by determining the level of hybridization complexes and then

calibrating said levels to determining levels of transcripts of the desired variant in the sample.

Both qualitative and quantitative determination methods can be used for diagnostic, prognostic and therapy planning purposes.

5 By a preferred embodiment the probe is part of a nucleic acid chip used for detection purposes, i.e. the probe is a part of an array of probes each present in a known location on a solid support.

The nucleic acid sequence used in the above method may be a DNA sequence an RNA sequence, etc; it may be a coding or a sequence or a sequence  
10 complementary thereto (for respective detection of RNA transcripts or coding-DNA sequences). By quantization of the level of hybridization complexes and calibrating the quantified results it is possible also to detect the level of the transcript in the sample.

Methods for detecting mutations in the region coding for the variant product  
15 are also provided, which may be methods carried-out in a binary fashion, namely merely detecting whether there is any mismatches between the normal variant nucleic acid sequence of the invention and the one present in the sample, or carried-out by specifically detecting the nature and location of the mutation.

The present invention also concerns a method for detecting variant product  
20 in a biological sample, comprising the steps of:

(a) contacting with said biological sample the antibody of the invention, thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the  
25 presence of variant product in said biological sample.

Many diseases are diagnosed by detecting the presence of antibodies against a protein characterizing the disease in the blood, serum or any other body fluid of the patient. The present invention also concerns a method for detecting anti-variant antibody in a biological sample, comprising:

(a) contacting said sample with the variant product of the invention, thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the  
5 presence of anti-variant antibody in the sample.

As indicated above, both methods (for detection of variant product and for detection of the anti-variant antibody) can be quantitized to determine the level or the amount of the variant or antibody in the sample, alone or in comparison to the level of the original amino acid sequence from which it was varied or compared to  
10 the level of antibodies against the original amino acid sequence, and qualitative and quantitative results may be used for diagnostic, prognostic and therapy planning purposes.

The invention also concerns distinguishing antibodies, i.e. antibodies capable of binding either to the variant product or to the original sequence from  
15 which the variant has been varied, while not binding to the original sequence or the variant product respectively. These distinguishing antibodies may be used for detection purposes.

By yet another aspect the invention also provides a method for identifying candidate compounds capable of binding to the variant product and modulating its  
20 activity (being either activators or deactivators). The method includes:

(i) providing a protein or polypeptide comprising an amino acid sequence substantially as depicted in any one of SEQ ID NO: 88 to 174, or a fragment of such a sequence;

(ii) contacting a candidate compound with said amino acid sequence;

25 (iii) measuring the physiological effect of said candidate compound on the activity of the amino acid sequences and selecting those compounds which show a significant effect on said physiological activity.

The present invention also concerns compounds identified by the above methods described above, which compound may either be an activator of the  
30 variant product or a deactivator thereof.

## BRIEF DESCRIPTION OF THE DRAWINGS

In order to understand the invention and to see how it may be carried out in practice, a preferred embodiment will now be described, by way of non-limiting example only, with reference to the accompanying drawings, in which:

5       **Fig. 1** is a comparison between the amino acid sequence of SEQ ID NO: 88 and the original sequence from which it has been varied;

**Fig. 2** is a comparison between the amino acid sequence of SEQ ID NO: 89 and the original sequence from which it has been varied;

**Fig. 3** is a comparison between the amino acid sequence of SEQ ID NO: 90  
10 and the original sequence from which it has been varied;

**Fig. 4** is a comparison between the amino acid sequence of SEQ ID NO: 91 and the original sequence from which it has been varied;

**Fig. 5** is a comparison between the amino acid sequence of SEQ ID NO: 92 and the original sequence from which it has been varied;

15       **Fig. 6** is a comparison between the amino acid sequence of SEQ ID NO: 93 and the original sequence from which it has been varied;

**Fig. 7** is a comparison between the amino acid sequence of SEQ ID NO: 94 and the original sequence from which it has been varied;

**Fig. 8** is a comparison between the amino acid sequence of SEQ ID NO: 95  
20 and the original sequence from which it has been varied;

**Fig. 9** is a comparison between the amino acid sequence of SEQ ID NO: 96 and the original sequence from which it has been varied;

**Fig. 10** is a comparison between the amino acid sequence of SEQ ID NO: 97 and the original sequence from which it has been varied;

25       **Fig. 11** is a comparison between the amino acid sequence of SEQ ID NO: 98 and the original sequence from which it has been varied;

**Fig. 12** is a comparison between the amino acid sequence of SEQ ID NO: 99 and the original sequence from which it has been varied;

**Fig. 13** is a comparison between the amino acid sequence of SEQ ID  
30 NO: 100 and the original sequence from which it has been varied;

**Fig. 14** is a comparison between the amino acid sequence of SEQ ID NO: 101 and the original sequence from which it has been varied;

**Fig. 15** is a comparison between the amino acid sequence of SEQ ID NO: 102 and the original sequence from which it has been varied;

5 **Fig. 16** is a comparison between the amino acid sequence of SEQ ID NO: 103 and the original sequence from which it has been varied;

**Fig. 17** is a comparison between the amino acid sequence of SEQ ID NO: 104 and the original sequence from which it has been varied;

**Fig. 18** is a comparison between the amino acid sequence of SEQ ID  
10 NO: 105 and the original sequence from which it has been varied;

**Fig. 19** is a comparison between the amino acid sequence of SEQ ID NO: 106 and the original sequence from which it has been varied;

**Fig. 20** is a comparison between the amino acid sequence of SEQ ID NO: 107 and the original sequence from which it has been varied;

15 **Fig. 21** is a comparison between the amino acid sequence of SEQ ID NO: 108 and the original sequence from which it has been varied;

**Fig. 22** is a comparison between the amino acid sequence of SEQ ID NO: 109 and the original sequence from which it has been varied;

**Fig. 23** is a comparison between the amino acid sequence of SEQ ID  
20 NO: 110 and the original sequence from which it has been varied;

**Fig. 24** is a comparison between the amino acid sequence of SEQ ID NO: 111 and the original sequence from which it has been varied;

**Fig. 25** is a comparison between the amino acid sequence of SEQ ID NO: 112 and the original sequence from which it has been varied;

25 **Fig. 26** is a comparison between the amino acid sequence of SEQ ID NO: 113 and the original sequence from which it has been varied;

**Fig. 27** is a comparison between the amino acid sequence of SEQ ID NO: 114 and the original sequence from which it has been varied;

**Fig. 28** is a comparison between the amino acid sequence of SEQ ID  
30 NO: 115 and the original sequence from which it has been varied;

Fig. 29 is a comparison between the amino acid sequence of SEQ ID NO: 116 and the original sequence from which it has been varied;

Fig. 30 is a comparison between the amino acid sequence of SEQ ID NO: 117 and the original sequence from which it has been varied;

5 Fig. 31 is a comparison between the amino acid sequence of SEQ ID NO: 118 and the original sequence from which it has been varied;

Fig. 32 is a comparison between the amino acid sequence of SEQ ID NO: 119 and the original sequence from which it has been varied;

10 Fig. 33 is a comparison between the amino acid sequence of SEQ ID NO: 120 and the original sequence from which it has been varied;

Fig. 34 is a comparison between the amino acid sequence of SEQ ID NO: 121 and the original sequence from which it has been varied;

Fig. 35 is a comparison between the amino acid sequence of SEQ ID NO: 122 and the original sequence from which it has been varied;

15 Fig. 36 is a comparison between the amino acid sequence of SEQ ID NO: 123 and the original sequence from which it has been varied;

Fig. 37 is a comparison between the amino acid sequence of SEQ ID NO: 124 and the original sequence from which it has been varied;

20 Fig. 38 is a comparison between the amino acid sequence of SEQ ID NO: 125 and the original sequence from which it has been varied;

Fig. 39 is a comparison between the amino acid sequence of SEQ ID NO: 126 and the original sequence from which it has been varied;

Fig. 40 is a comparison between the amino acid sequence of SEQ ID NO: 127 and the original sequence from which it has been varied;

25 Fig. 41 is a comparison between the amino acid sequence of SEQ ID NO: 128 and the original sequence from which it has been varied;

Fig. 42 is a comparison between the amino acid sequence of SEQ ID NO: 129 and the original sequence from which it has been varied;

30 Fig. 43 is a comparison between the amino acid sequence of SEQ ID NO: 130 and the original sequence from which it has been varied;

**Fig. 44** is a comparison between the amino acid sequence of SEQ ID NO: 131 and the original sequence from which it has been varied;

**Fig. 45** is a comparison between the amino acid sequence of SEQ ID NO: 132 and the original sequence from which it has been varied;

5 **Fig. 46** is a comparison between the amino acid sequence of SEQ ID NO: 133 and the original sequence from which it has been varied;

**Fig. 47** is a comparison between the amino acid sequence of SEQ ID NO: 134 and the original sequence from which it has been varied;

10 **Fig. 48** is a comparison between the amino acid sequence of SEQ ID NO: 135 and the original sequence from which it has been varied;

**Fig. 49** is a comparison between the amino acid sequence of SEQ ID NO: 136 and the original sequence from which it has been varied;

**Fig. 50** is a comparison between the amino acid sequence of SEQ ID NO: 137 and the original sequence from which it has been varied;

15 **Fig. 51** is a comparison between the amino acid sequence of SEQ ID NO: 138 and the original sequence from which it has been varied;

**Fig. 52** is a comparison between the amino acid sequence of SEQ ID NO: 139 and the original sequence from which it has been varied;

20 **Fig. 53** is a comparison between the amino acid sequence of SEQ ID NO: 140 and the original sequence from which it has been varied;

**Fig. 54** is a comparison between the amino acid sequence of SEQ ID NO: 141 and the original sequence from which it has been varied;

**Fig. 55** is a comparison between the amino acid sequence of SEQ ID NO: 142 and the original sequence from which it has been varied;

25 **Fig. 56** is a comparison between the amino acid sequence of SEQ ID NO: 143 and the original sequence from which it has been varied;

**Fig. 57** is a comparison between the amino acid sequence of SEQ ID NO: 144 and the original sequence from which it has been varied;

30 **Fig. 58** is a comparison between the amino acid sequence of SEQ ID NO: 145 and the original sequence from which it has been varied;

Fig. 59 is a comparison between the amino acid sequence of SEQ ID NO: 146 and the original sequence from which it has been varied;

Fig. 60 is a comparison between the amino acid sequence of SEQ ID NO: 147 and the original sequence from which it has been varied;

5 Fig. 61 is a comparison between the amino acid sequence of SEQ ID NO: 148 and the original sequence from which it has been varied;

Fig. 62 is a comparison between the amino acid sequence of SEQ ID NO: 149 and the original sequence from which it has been varied;

Fig. 63 is a comparison between the amino acid sequence of SEQ ID NO: 10 150 and the original sequence from which it has been varied;

Fig. 64 is a comparison between the amino acid sequence of SEQ ID NO: 151 and the original sequence from which it has been varied;

Fig. 65 is a comparison between the amino acid sequence of SEQ ID NO: 152 and the original sequence from which it has been varied;

15 Fig. 66 is a comparison between the amino acid sequence of SEQ ID NO: 153 and the original sequence from which it has been varied;

Fig. 67 is a comparison between the amino acid sequence of SEQ ID NO: 154 and the original sequence from which it has been varied;

Fig. 68 is a comparison between the amino acid sequence of SEQ ID NO: 20 155 and the original sequence from which it has been varied;

Fig. 69 is a comparison between the amino acid sequence of SEQ ID NO: 156 and the original sequence from which it has been varied;

Fig. 70 is a comparison between the amino acid sequence of SEQ ID NO: 157 and the original sequence from which it has been varied;

25 Fig. 71 is a comparison between the amino acid sequence of SEQ ID NO: 158 and the original sequence from which it has been varied;

Fig. 72 is a comparison between the amino acid sequence of SEQ ID NO: 159 and the original sequence from which it has been varied;

Fig. 73 is a comparison between the amino acid sequence of SEQ ID NO: 30 160 and the original sequence from which it has been varied;



**Fig. 74** is a comparison between the amino acid sequence of SEQ ID NO: 161 and the original sequence from which it has been varied;

**Fig. 75** is a comparison between the amino acid sequence of SEQ ID NO: 162 and the original sequence from which it has been varied;

5       **Fig. 76** is a comparison between the amino acid sequence of SEQ ID NO: 163 and the original sequence from which it has been varied;

**Fig. 77** is a comparison between the amino acid sequence of SEQ ID NO: 164 and the original sequence from which it has been varied;

**Fig. 78** is a comparison between the amino acid sequence of SEQ ID NO: 10 165 and the original sequence from which it has been varied;

**Fig. 79** is a comparison between the amino acid sequence of SEQ ID NO: 166 and the original sequence from which it has been varied;

**Fig. 80** is a comparison between the amino acid sequence of SEQ ID NO: 167 and the original sequence from which it has been varied;

15       **Fig. 81** is a comparison between the amino acid sequence of SEQ ID NO: 168 and the original sequence from which it has been varied;

**Fig. 82** is a comparison between the amino acid sequence of SEQ ID NO: 169 and the original sequence from which it has been varied;

**Fig. 83** is a comparison between the amino acid sequence of SEQ ID NO: 20 170 and the original sequence from which it has been varied;

**Fig. 84** is a comparison between the amino acid sequence of SEQ ID NO: 171 and the original sequence from which it has been varied;

**Fig. 85** is a comparison between the amino acid sequence of SEQ ID NO: 172 and the original sequence from which it has been varied;

25       **Fig. 86** is a comparison between the amino acid sequence of SEQ ID NO: 173 and the original sequence from which it has been varied;

**Fig. 87** is a comparison between the amino acid sequence of SEQ ID NO: 174 and the original sequence from which it has been varied;

Fig. 88 shows immunohistochemical staining with antibodies against a fragment of the ACEV product of SEQ ID NO: 144; expressed in ductal epitelus in salivatory gland (magnification X 100);

Fig. 89 shows the same as in Fig. 89 (magnification X 400);

5 Fig. 90 shows immunohistochemical staining with antibodies against a fragment of ACEV product of SEQ ID NO: 144 expressed in salivary glands surrounding the lymph nodes; and

Fig. 91 shows RT-PCR results of the ACEV sequence expressed in salivary glands.

10

## DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

### Example I: Comparison of variants with original sequences

Original sequences were obtained from GenBank Version 110. Comparison between the original sequences and the novel variant sequences was  
15 made using the Pileup application from the GCG suite version 10.0 (January 1999), with the default values:

Gap creation penalty (GapWeight): 8

Gap extension penalty (GapLengthWeight): 2

The comparison is shown in Fig. 1 to 87 which show the comparison of  
20 each of the variant products depicted in SEQ ID NO: 88 to 174 with the original sequence from which it was varied.

The following is a list which gives the name and the description of each original sequence from which the alternative splice variant has been varied by alternative splicing. The description is followed by the internal reference to the  
25 novel variant (NV-NV... or NV-... etc.) and a short comparison between the variant and the original sequence. It should be noticed that several splice variants may have been originated from the same parent sequence by several different alternative splicings. The following table summarizes the accession number of the original sequence, the terminology of the new variant (RN-NV... or NV-...) and  
30 the description of the difference between the new variant and the original sequence.

Table

Accession	SEQ ID NO:	Description of the New Variant
AA2A_HUMAN	88	Gap between amino acids at the positions 237-247 of the original protein. Missing 6th transmembrane loop of the original Adenosine A2 receptor.
ASM_HUMAN	89	Insertion of 2 amino acids after amino acid at the position 34 and insertion of 54 amino acids after amino acid at the position 492 of the original SPHINGOMYELIN PHOSPHODIESTERASE protein.
FA12_HUMAN	90	Alternative 10 C-terminal amino acids. Has part of catalytic domain missing 1 active site.
GCSR_HUMAN	91	Deletion of 62 amino acids between the positions 320-382 of the original GRANULOCYTE COLONY STIMULATING FACTOR receptor. The deletion is in the EXTRACELLULAR domain in one of the FIBRONECTIN TYPE-III domains R1.
GCSR_HUMAN	92	Insertion of 37 amino acids in the extracellular domain after the position 574 of the original GRANULOCYTE COLONY STIMULATING FACTOR receptor.
GLR2_HUMAN	93	Replacement of 88 C-terminal amino acids of the original glutamate receptor 2 by alternative 42 amino acids. Has most of domains, might be missing 4th transmembrane domain.
GLUC_HUMAN	94	Gap; 156aa compared to 180aa; exact 1-108; gap 108-132; exact 132-180. Missing almost whole GLUCAGON-LIKE PEPTIDE 1
IHBA_HUMAN	95	Replacement of 128 N-terminal amino acids of the original inhibin protein by alternative 5 amino acids. The deleted part contains propep and glycosylation site of the original protein. The resulting new variant sustains the inhibin beta chain.
IL6_HUMAN	96	Deletion of 17 amino acids between the positions 79-96 of the original interleukin 6 protein. Has all necessary domains.
IL6_HUMAN	97	Deletion of 55 amino acids between the positions 6-61 of the original protein. Has only the beginning of signal peptide; has disulfide bonds and carbohydrate region.
REL1_HUMAN	98	Insertion of 35 amino acids after the amino acid

		at the position 70 of the original relaxin protein. The insertion is in the connecting peptide.
SY04_HUMAN	99	Deletion of 5 amino acids between the positions 65-69 of the original protein. Replacement of the amino acid at the position 70 of the original protein by an alternative amino acid. Missing part of strand.
TSP1_HUMAN	100	Truncated: exact 1-722 (731aa long compared to 1170aa), last 9 amino acids are different. Missing 7 X TSP TYPE-3-REPEATS CA-BINDING domain C-TERMINAL, missing CELL ATTACHMENT SITE, missing 1 out of 4 glycosylation sites. Has all other components including signal peptide.
TSP1_HUMAN	101	Truncated exact 1-548 (555aa long compared to 1170) last 7aa different. Missing 3 X EGF-TYPE REPEATS, missing 7 X TSP TYPE-3 REPEATS Ca-BINDING domain C-TERMINAL missing CELL ATTACHMENT SITE, missing all diSulfide bonds, missing 2 out of 4 glycosylation sites. Has all other domains (including signal peptide).
TSP1_HUMAN	102	Truncated: exact 1-490 (546aa long compared to 1170) last 56 amino acids are different. Missing 1 out of 3 X TXP TYPE-1 REPEATS (CS-LIKE), Missing 3 X EGF-TYPE REPEATS, missing 7 X TSP TYPE-3 REPEATS CA-BINDING domain C-TERMINAL missing CELL ATTACHMENT SITE, missing all diSulfide bonds, missing 2 out of 4 glycosylations. Has all other domains (including signal peptide).
TSP1_HUMAN	103	Truncated: exact 1-431aa (459aa long compared to 1170) last 28 amino acids are different. Missing 2 out of 3 X TSP TYPE-1 REPEATS (CS-LIKE), Missing 3 X EGF-TYPE REPEATS, missing 7 X TSP TYPE-3 REPEATS CA-BINDING domain C-TERMINAL missing CELL ATTACHMENT SITE, missing all disulfide bonds, missing 2 out of 4 glycosylations. Has all other domains (including signal peptide).
TYPH_HUMAN	104	Deletion of 119 amino acids between the positions 33-452 of the original protein. The resulting new variant is missing the 3 <sup>rd</sup> repeat of the original protein.

TYPH_HUMAN	105	Replacement of 48 amino acids between the positions 216-264 of the original protein by alternative 9 amino acids.
TYPH_HUMAN	106	Deletion of 119 amino acids between the positions 333-452, missing 3 <sup>rd</sup> repeat of the original protein. Replacement of 48 amino acids between the positions 216-264 of the original protein by alternative 9 amino acids.
IC1_HUMAN	107	Deletion of 19 amino acids between the positions 29-48 of the original protein. Missing 1 glycosylation out of 14.
PT16_HUMAN	108	Deletion of 261 N-terminal amino acids of the original protein (the first possible Met is at the position 261). The new variant has 116 amino acids compared to 376 in the original protein (exact 261-376), including the active site.
PT16_HUMAN	109	Deletion of 57 amino acids between the positions 267-325 of the original protein. The resulting new variant contains the active site.
PT16_HUMAN	110	Deletion of 189 amino acids between the positions 89-278 of the original protein. The resulting new variant contains the active site.
PT16_HUMAN	111	Replacement of 376 C-terminal amino acids of the original protein by alternative 5 amino acids. The resulting new variant doesn't contain the active site.
IAP2_HUMAN	112	Truncated: 305 amino acids compared to 618 aa (protein 2). The new variant contains exact positions 1-299, last 6 amino acids are different. Two SNIPs in position 235 and 241 of the original protein. The new variant is missing Zn Finger and half of 3 <sup>rd</sup> BIR repeat.
SET_HUMAN	113	Extra 83 amino acids in the N-terminus of the protein. The added sequence has predicted potential transmembrane domain (probable signal peptide?)
SET_HUMAN	114	Replacement of 24 C-terminal amino acids of the original protein by alternative 8 amino acids. Missing part of ASP/GLU-RICH and BREAKPOINT FOR TRANSLOCATION TO FORM SET-CAN ONCOGENE.
CDNC_HUMAN	115	Deletion of 178 amino acids at the positions 97-275 of the original protein. Insertion of 121 amino acids at the N-terminus. The resulting new variant is missing PAPA repeats.
F13B_MOUSE	116	Deletion of 87 C-terminal amino acids of the original protein. SNIP at position 236 (L->V). The resulting new variant is missing the last

		shushi repeat.
EGF_MOUSE	117	Deletion of 641 amino acids between the positions 67-708 of the original protein. Missing 4 EGF-like domains, 2 glycosylations, 9 diSulfide bonds.
EGF_MOUSE	118	Deletion of 641 amino acids between the positions 67-708, and deletion of 45 amino acids between the positions 1020-1065 of the original protein. Missing 4 EGF-like domains, 2 glycosylations, 9 diSulfide bonds. Missing transmembrane domain.
EGF_MOUSE	119	Deletion of 641 amino acids between the positions 67-708 of the original protein. Missing 4 EGF-like domains, 2 glycosylations, 9 diSulfide bonds. Replacement of 419 C-terminal amino acids by 5 amino acids.
EGF_MOUSE	120	Deletion of 841 amino acids between the positions 18-859 of the original protein. Missing 5 EGF-like domains and 2 glycosylation sites.
EGF_MOUSE	121	Deletion of 774 amino acids between the positions 5-779 of the original protein. Missing signal peptide, 5 EGF-like domains, and 2 glycosylation sites.
P53_MOUSE	122	Deletion of 336 N-terminal amino acids of the original protein. Missing ASP/GLU-RICH (ACIDIC), missing hydrophobic domain, missing NUCLEAR LOCALIZATION SIGNAL, missing 1 out of 2 PHOSPHORYLATION sites.
NME3_HUMAN	123	Deletion of 381 N-terminal amino acids of the original protein. Missing 2 out of 4 glycosylation sites.
TRFE_HUMAN	124	Deletion of 34 amino acids between the positions 654-689 of the original protein. Loss of disulfide bond.
TRFE_HUMAN	125	Deletion of 52 amino acids between the positions 447-499 of the original protein. Loss of disulfide bond.
BAA23795	126	Replacement of 83 C-terminal amino acids from probable cytoplasmic domain of the original protein by alternative 4 amino acids. Resulting in truncated new variant: 4787 compared to 4866, exact 1-4783 with last 4 amino acids different.
VIPS_HUMAN	127	Replacement of 64 C-terminal amino acids of the original protein by alternative 7 amino acids. The resulting new variant is missing the

		last transmembrane and the cytoplasmic domains.
PACR_HUMAN	128	Deletion of 22 amino acids between the positions 88-110 of the original protein. The deletion is an extracellular loop.
NRP_HUMAN	129	Deletion of 540 C-terminal amino acids of the original protein, resulting in truncated new variant (383 compared to 923 amino acids). The new variant is missing part of the extracellular domain, the cytoplasmic and the transmembrane domains.
NRP_HUMAN	130	Replacement of 595 C-terminal amino acids of the original protein by alternative 11 amino acids. The resulting new variant is truncated (339 compared to 923 amino acids, exact 1-328 with last 11 amino acids different), and is missing part of the extracellular domain, the cytoplasmic and the transmembrane domains.
gi1899200	131	Deletion of 114 amino acids between the positions 1257-1372 of the original N-METHYL D-ASPARTATE RECEPTOR SUBTYPE 2A protein.
VIPS_HUMAN	132	Replacement of 56 C-terminal amino acids from the cytoplasmic domain of the original protein by alternative 73 amino acids.
VIPS_HUMAN	133	Replacement of 56 C-terminal amino acids from the cytoplasmic domain of the original protein by alternative 70 amino acids.
IG1R_HUMAN	134	Deletion of 22 amino acids between the positions 1268-1291 of the original protein. The deleted fragment is part of the cytoplasmic domain of INSULIN-LIKE GROWTH FACTOR I RECEPTOR, BETA-CHAIN.
NRP_HUMAN	135	Replacement of 282 C-terminal amino acids of the original protein, including the transmembrane domain and the MAM domain, by alternative 3 amino acids.
NRP_HUMAN	136	Deletion of 83 amino acids between the positions 538-622 of the original protein. The deleted region includes part of the F5/8 TYPE C 2 domain and part of the MAM domain.
NRP_HUMAN	137	Deletion of 385 C-terminal amino acids of the original protein, including the transmembrane domain and the MAM domain.
FGR3_HUMAN	138	Replacement of 496 C-terminal amino acids of the original protein by alternative 79 amino acids.. The deleted region includes the C-terminal part of the extracellular domain, the

		transmembrane domain, the cytoplasmic domain, the protein kinase domain and the two ATP binding domains.
F13B_MOUSE	139	Replacement of 340 aa of the c-terminus of the original protein in 3aa deletion of sushi 6-10 domain
EGF_MOUSE	140	Deletion of 144 amino acids between the positions 1020-1165, including the transmembrane domain and part of the cytoplasmic domain of the original protein.
EGF_MOUSE	141	Replacement of 418 C-terminal amino acids of the original protein by alternative 5 amino acids. The deleted region includes the EGF active chain, 4 out of 9 EGF-like domains within the extracellular region of the protein, the transmembrane and the cytoplasmic regions.
EGF_MOUSE	142	Deletion of 641 amino acids between the positions 66-707 of the original protein. The deleted region is in the extracellular part of the protein and it includes 4 out of 9 EGF-like domains. NV-20 contains the original signal peptide, part of the extracellular domain, the epidermal growth factor chain (located between the positions 977-1029 of the original protein), and the original transmembrane and the cytoplasmic domains.
EGF_MOUSE	143	Deletion of 842 amino acids between the positions 17-859 of the original protein (including replacement of the amino acid in the position 859 by an alternative one). The deleted region is in the extracellular part of the protein and it includes 5 out of 9 EGF-like domains. NV-20 contains the original signal peptide, part of the extracellular domain, the epidermal growth factor chain (located between the positions 977-1029 of the original protein), and the original transmembrane and the cytoplasmic domains.
ACE_MOUSE	144	Replacement of 77 C-terminal amino acids of the original protein, including the entire transmembrane and cytoplasmic domains, by alternative 14 amino acids.
ESR1_MOUSE	145	Replacement of 229 C-terminal amino acids of the original protein, including part of the steroid-binding domain, by alternative 12 amino acids.
FA7_MOUSE	146	Deletion of 101 amino acids, between the positions 119-220 of the original protein. The



		deleted region contains 74 amino acids from the C-terminal end of the factor VII light chain, and 26 amino acids from the N-terminal end of the factor VII heavy catalytic chain. The deleted region includes EGF-like 2 domain and the cleavage site (by factor XA, factor XIIA, factor IXA, or thrombin) of the original protein.
CAL0_MOUSE	147	Deletion of 33 amino acids, spanning the positions 18-50, between the signal and the calcitonin peptide in the original precursor protein.
Gi 2826776	148	Replacement of the last 7 C-terminal amino acids of the original protein by alternative 11 amino acids.
PTI6_HUMAN	149	Replacement of the last 4 C-terminal amino acids of the original protein by alternative 28 amino acids.
PTI6_HUMAN	150	Replacement of the last 16 C-terminal amino acids of the original protein by alternative 12 amino acids.
_RIN1_HUMAN	151	Replacement of 158 last C-terminal amino acids of the original protein by alternative 71 amino acids with probable transmembrane region.
CDNC_HUMAN	152	Addition of 121 amino acids at the N-terminus of the protein.
CDN2_HUMAN	153	Replacement of 5 amino acids at the positions 18, 24, 27, 30, 37 of the original protein by alternative amino acids. Replacement of last 4 C-terminal amino acids of the original protein by alternative 20 amino acids.
CDN5_HUMAN	154	Replacement of the last 6 C-terminal amino acids of the original protein by alternative 52 amino acids.
HEP2_HUMAN	155	Deletion of 150 amino acids, between the positions 334-485, of the original protein. The deleted region includes the reactive bond (the active site) of the original protein. NV-33 does contain the chemotactic activity domain, the glycosaminoglycan-binding site and the hirudin-like 2 x 11 AA approximate repeats, Asp/Glu rich.
TFP2_HUMAN	156	Replacement of 36 C-terminal amino acids of the original protein by alternative 12 amino acids. The deleted region includes part of the BPTI/KUNITZ inhibitor domain-3 and the poly-Lysine domain of the original protein.
TFP2_HUMAN	157	Deletion of 25 amino acids, between the positions 153-178 of the original protein, and

		replacement of the amino acid at the position 179 by alternative one. The deleted region includes the active site and part of the BPTI/KUNITZ inhibitor domain-3.
TFPI_HUMAN	158	Replacement of 95 C-terminal amino acids of the original protein, containing the entire BPTI/KUNITZ inhibitor-3 domain, by alternative 16 amino acids.
IC1_HUMAN	159	Insertion of 136 aa at position 227 of the original protein.
PTI6_HUMAN	160	Replacement of last 15 aa in the original protein in 28 aa, the cds of the NV has no stop codon.
PTI6_HUMAN	161	Replacement of last 185 aa of the original protein in 13 aa. The NV lacks the ACT site.
PTI6_HUMAN	162	Replacement of last 230 aa of the original protein in 10 aa. The NV lacks the ACT site.
TYPH_HUMAN	163	Insertion of 35 aa at position 387 of the original protein.
CDNC_HUMAN	164	Replacement of 220 aa of the c-terminus of the original protein in 47 aa. Deletion of all 9 x 4 aa repeats of p-a-p-a. Deletion of the potential nuclear localization signal (278-281 in the original protein).
FGR3_HUMAN	165	Replacement of 264 aa of the c-terminus of the original protein in 19 aa. Deletion of part of the potential cytoplasmatic protein (397-806 in the original protein), part of the protein kinase domain (472-761), deletion of the ACT site (617).
TFP2_HUMAN	166	Replacement of 58 aa of the c-terminus of the original protein in 12 aa. Deletion of part of the bpti/kunitz inhibitor 3 domain (158-208 in the original protein).
TRFE_HUMAN	167	Insertion of 32 aa at position 366 of the original protein.
VIPS_HUMAN	168	Replacement of 388 aa of the c-terminus of the original protein in 27 aa. Deletion of all potential 7 trans membrana domain.
TFPI_HUMAN	169	Replacement of 180 aa of the n-terminus of the original protein in 37 aa. Deletion of the signal peptide and deletion of the bpti/kunitz inhibitor 1 and 2 domains.
P53_MOUSE	170	Replacement of 246 aa of the n-terminus of

- 36 -

		the original protein in 13 aa. Deletion of the asp/glu-rich (acidic) domain.
P53_MOUSE	171	Replacement of 246 aa of the n-terminus of the original protein in 13 aa. Deletion of the asp/glu-rich (acidic) domain.
ACE_MOUSE	172	Replacement of 77 aa of the c-terminus of the original protein in 17 aa. Deletion of the entire transmembrane and cytoplasmatic domains.
ESR1_MOUSE	173	Deletion of 225 aa of the c-terminus of the original protein. Deletion of most of the steroid binding domain (315-599 in the original protein). RT-PCR results implies that the NV exhibits similarity to thr somatic ACE (results not shown).
vesicular GABA and glycine transporter (mouse), gi 2826776	174	Replacement of 73 aa of the c-terminus of the original protein in 21 aa.

### Identification of the original sequence from which the novel Variant was variant

5           The following is the explanation of the definition to be used in the following:

10           **Accession:**           Accession number of the original sequence in the GeneBank database  
**Name:**                   Name of the original sequence in the database  
**Function:**               Physiological activity.

### SEQ ID NO : Sequence number of variant

15           **Description:**           the difference between the variant and the original sequence.

20           **Accession:**           AA2A\_HUMAN  
**Name:**                   Adenosine A2 receptor  
**Function:**               Receptor for adenosine.

SEQ ID 1

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**Description:** Gap between amino acids at the positions 237-247 of the original protein. Missing 6th transmembrane loop of the original Adenosine A2 receptor.

5 **Accession:** ASM\_HUMAN  
**Name:** SPHINGOMYELIN PHOSPHODIESTERASE  
**Function:** Converts sphingomyelin to ceramide.

**SEQ ID : 2**

10

**Description:** Insertion of 2 amino acids after amino acid at the position 34 and insertion of 54 amino acids after amino acid at the position 492 of the original SPHINGOMYELIN PHOSPHODIESTERASE protein.

15 **Accession:** FA12\_HUMAN  
**Name:** COAGULATION FACTOR XII  
**Function:** Factor XII is a serum glycoprotein that participates in the initiation of blood coagulation, fibrinolysis, and the generation of bradykinin and angiotensin.

20

**SEQ ID : 3**

**Description:** Alternative 10 C-terminal amino acids. Has part of catalytic domain missing 1 active site.

25

**Accession:** GCSR\_HUMAN  
**Name:** GRANULOCYTE COLONY STIMULATING FACTOR receptor  
**Function:** Receptor for granulocyte colony-stimulating factor (g- csf). In addition it may function in some adhesion or recognition events at the cell surface.

30

**SEQ ID : 4**

35 **Description:** Deletion of 62 amino acids between the positions 320-382 of the original GRANULOCYTE COLONY STIMULATING FACTOR receptor.

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The deletion is in the EXTRACELLULAR domain in one of the FIBRONECTIN TYPE-III domains R1.

**Accession:** GCSR\_HUMAN  
5 **Name:** GRANULOCYTE COLONY STIMULATING FACTOR  
receptor  
**Function:** Receptor for granulocyte colony-stimulating factor (g- csf).  
In addition it may function in some adhesion or recognition  
events at the cell surface.

10

**SEQ ID : 5**

**Description:** Insertion of 37 amino acids in the extracellular domain after the  
position 574 of the original GRANULOCYTE COLONY STIMULATING  
15 **FACTOR** receptor.

**Accession:** GLR2\_HUMAN  
**Name:** Glutamate receptor 2  
**Function:** L-glutamate acts as an excitatory neurotransmitter at many  
20 synapses in the central nervous system. the postsynaptic  
actions of Glu are mediated by a variety of receptors are  
named according to their selective agonists

**SEQ ID : 6**

25

**Description:** Replacement of 88 C-terminal amino acids of the original  
glutamate receptor 2 by alternative 42 amino acids. Has most of domains, might  
be missing 4th transmembrane domain.

30 **Accession:** GLUC\_HUMAN  
**Name:** Glucagon  
**Function:** Promotes hydrolysis of glycogen and lipids, and raises the  
blood sugar level.

35 **SEQ ID : 7**

- 39 -

**Description** Gap; 156aa compared to 180aa; exact 1-108; gap 108-132; exact 132-180. Missing almost whole GLUCAGON-LIKE PEPTIDE 1

**Accession:** IHBA\_HUMAN

5 **Name:** Inhibin; erythroid differentiation factor

**Function:** Inhibin is a gonadal glycopeptide that inhibits the secretion of follitropin by the pituitary gland. On the other hand activin activates the secretion of follitropin. Activin is also important in embryonic axial development.

10

**SEQ ID : 8**

**Description:** Replacement of 128 N-terminal amino acids of the original inhibin protein by alternative 5 amino acids. The deleted part contains propep and  
15 glycosylation site of the original protein. The resulting new variant sustains the inhibin beta chain.

**Accession:** IL6\_HUMAN

**Name:** Interleukin 6

20 **Function:** IL-6 is a cytokine with a wide variety of biological functions: it plays an essential role in the final differentiation of B-cells into Ig-secreting cells, it induces myeloma and plasmacytoma growth, it induces nerve cells differentiation.

25 **SEQ ID : 9**

**Description:** Deletion of 17 amino acids between the positions 79-96 of the original interleukin 6 protein. Has all necessary domains.

30 **Accession:** IL6\_HUMAN

**Name:** Interleukin 6

**Function:** IL-6 is a cytokine with a wide variety of biological functions: it plays an essential role in the final differentiation of B-cells into Ig-secreting cells, it induces myeloma  
35 and plasmacytoma growth, it induces nerve cells differentiation.

- 40 -

**SEQ ID : 10**

**Description:** Deletion of 55 amino acids between the positions 6-61 of the original protein. Has only the beginning of signal peptide; has disulfide bonds and carbohydrate region.

**Accession:** REL1\_HUMAN

**Name:** Relaxin

**Function:** Relaxin is an ovarian hormone that acts with estrogen to produce dilatation of the birth canal in many mammals.

**SEQ ID : 11**

**Description:** Insertion of 35 amino acids after the amino acid at the position 70 of the original relaxin protein. The insertion is in the connecting peptide.

**Accession:** SY04\_HUMAN

**Name:** SMALL INDUCIBLE CYTOKINE A4, MACROPHAGE INFLAMMATORY PROTEIN 1-BETA

**Function:** Monokine with inflammatory and chemokinetic properties

**SEQ ID : 12**

**Description:** Deletion of 5 amino acids between the positions 65-69 of the original protein. Replacement of the amino acid at the position 70 of the original protein by an alternative amino acid. Missing part of strand.

**Accession:** TSP1\_HUMAN

**Name:** Thrombospondin adhesive glycoprotein

**Function:** Adhesive glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. Can bind to fibrinogen, fibronectin, laminin and type v collagen

**SEQ ID : 13**

**Description:** Truncated exact 1-722 (731aa long compared to 1170aa), last 9 amino acids are different. Missing 7 X TSP TYPE-3 REPEATS CA-BINDING

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domain C-TERMINAL, missing CELL ATTACHMENT SITE, missing 1 out of 4 glycosylation sites. Has all other components including signal peptide

**Accession:** TSP1\_HUMAN

5 **Name:** Thrombospondin adhesive glycoprotein

**Function:** Adhesive glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. Can bind to fibrinogen, fibronectin, laminin and type v collagen

10 **SEQ ID : 14**

**Description:** Truncated exact 1-548 (555aa long compared to 1170) last 7aa different. Missing 3 X EGF-TYPE REPEATS, missing 7 X TSP TYPE-3 REPEATS Ca-BINDING domain C-TERMINAL missing CELL  
15 ATTACHMENT SITE, missing all diSulfide bonds, missing 2 out of 4 glycosylation sites. Has all other domains (including signal peptide).

**Accession:** TSP1\_HUMAN

**Name:** Thrombospondin adhesive glycoprotein

20 **Function:** Adhesive glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. Can bind to fibrinogen, fibronectin, laminin and type v collagen

**SEQ ID : 15**

25 **Description:** Truncated exact 1-490 (546aa long compared to 1170) last 56 amino acids are different. Missing 1 out of 3 X TSP TYPE-1 REPEATS (CS-LIKE), Missing 3 X EGF-TYPE REPEATS, missing 7 X TSP TYPE-3 REPEATS CA-BINDING domain C-TERMINAL missing CELL  
30 ATTACHMENT SITE, missing all diSulfide bonds, missing 2 out of 4 glycosylations. Has all other domains (including signal peptide).

**Accession:** TSP1\_HUMAN

**Name:** Thrombospondin adhesive glycoprotein

35 **Function** Adhesive glycoprotein that mediates cell-to-cell and cell-to-matrix interactions. Can bind to fibrinogen, fibronectin, laminin and type v collagen



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**SEQ ID : 16**

**Description:** Truncated: exact 1-431aa (459aa long compared to 1170) last 28  
5 amino acids are different. Missing 2 out of 3 X TSP TYPE-1 REPEATS  
(CS-LIKE), Missing 3 X EGF-TYPE REPEATS, missing 7 X TSP TYPE-3  
REPEATS CA-BINDING domain C-TERMINAL missing CELL  
ATTACHMENT SITE, missing all diSulfide bonds, missing 2 out of 4  
glycosylations. Has all other domains (including signal peptide).

10

**Accession:** TYPH\_HUMAN

**Name:** PLATELET-DERIVED ENDOTHELIAL CELL GROWTH  
FACTOR

15

**Function:** May have a role in maintaining the integrity of the blood  
vessels. Has growth promoting activity on endothelial cells,  
angiogenic activity in vivo and chemotactic activity on  
endothelial cells *in vitro*.

20

CATALYSES THE REVERSIBLE PHOSPHOROLYSIS  
OF THYMIDINE. THE PRODUCED MOLECULES ARE  
THEN UTILIZED AS CARBON AND ENERGY  
SOURCES OR IN THE RESCUE OF PYRIMIDINE  
BASES FOR NUCLEOTIDE SYNTHESIS.

25

SIMILARITY: BELONGS TO THYMIDINE/  
PYRIMIDINE-NUCLEOSIDE PHOSPHORYLASES  
FAMILY.

**SEQ ID : 17**

30 **Description:** Deletion of 119 amino acids between the positions 333-452 of  
the original protein. The resulting new variant is missing the 3rd repeat of the  
original protein.

**Accession:** TYPH\_HUMAN

35 **Name:** PLATELET-DERIVED ENDOTHELIAL CELL GROWTH  
FACTOR

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**Function:** May have a role in maintaining the integrity of the vessels.  
Has growth promoting activity on endothelial cells,  
angiogenic activity in vivo and chemotactic activity on  
endothelial cells *in vitro*.

5 CATALYSES THE REVERSIBLE PHOSPHOROLYSIS  
OF THYMIDINE. THE PRODUCED MOLECULES ARE  
THEN UTILIZED AS CARBON AND ENERGY  
SOURCES OR IN THE RESCUE OF PYRIMIDINE  
BASES FOR NUCLEOTIDE SYNTHESIS.

10 SIMILARITY: BELONGS TO THYMIDINE/  
PYRIMIDINE-NUCLEOSIDE PHOSPHORYLASES  
FAMILY.

**SEQ ID : 18**

15 **Description:** Replacement of 48 amino acids between the positions 216-264  
of the original protein by alternative 9 amino acids.

**Accession:** TYPH\_HUMAN

20 **Name:** PLATELET-DERIVED ENDOTHELIAL CELL GROWTH  
FACTOR

**Function:** May have a role in maintaining the integrity of the vessels.  
Has growth promoting activity on endothelial cells,  
angiogenic activity in vivo and chemotactic activity on  
endothelial cells *in vitro*.

25 CATALYSES THE REVERSIBLE PHOSPHOROLYSIS  
OF THYMIDINE. THE PRODUCED MOLECULES ARE  
THEN UTILIZED AS CARBON AND ENERGY  
SOURCES OR IN THE RESCUE OF PYRIMIDINE  
BASES FOR NUCLEOTIDE SYNTHESIS.

30 SIMILARITY: BELONGS TO THYMIDINE/  
PYRIMIDINE-NUCLEOSIDE PHOSPHORYLASES  
FAMILY.

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**SEQ ID : 19**

**Description:** Deletion of 119 amino acids between the positions 333-452, missing 3rd repeat of the original protein. Replacement of 48 amino acids  
5 between the positions 216-264 of the original protein by alternative 9 amino acids.

**Accession:** IC1\_HUMAN

**Name:** PLASMA PROTEASE C1 INHIBITOR

10 **Function:** Activation of the c1 complex is under control of the c1-Inhibitor. IT FORMS A PROTEOLYTICALLY INACTIVE STOICHIOMETRIC COMPLEX WITH THE C1R OR C1S PROTEASES. MAY PLAY A POTENTIALLY CRUCIAL  
15 ROLE IN REGULATING IMPORTANT PHYSIOLOGICAL PATHWAYS INCLUDING COMPLEMENT ACTIVATION, BLOOD COAGULATION, FIBRINOLYSIS AND THE GENERATION OF KININS.  
PTM: HIGHLY GLYCOSYLATED (49%).  
20 SIMILARITY: BELONGS TO THE SERPIN FAMILY.

**SEQ ID NO : 20**

**Description:** Deletion of 19 amino acids between the positions 29-48 of the  
25 original protein. Missing 1 glycosylation out of 14.

**Accession:** PTI6\_HUMAN

**Name:** PLACENTAL THROMBIN INHIBITOR

**Function:** Cytoplasmic antiproteinase.  
30 SIMILARITY: BELONGS TO THE SERPIN FAMILY. OV-SERPIN SUBFAMILY.

**SEQ ID : 21**

35 **Description:** Deletion of 261 N-terminal amino acids of the original protein (the first possible Met is at the position 261). The new variant has 116 amino

- 45 -

acids compared to 376 in the original protein (exact 261-376), including the active site.

**Accession:** PTI6\_HUMAN

**Name:** PLACENTAL THROMBIN INHIBITOR

5 **Function:** Cytoplasmic antiproteinase  
SIMILARITY: BELONGS TO THE SERPIN FAMILY.  
OV-SERPIN SUBFAMILY.

**SEQ ID : 22**

10

**Description:** Deletion of 57 amino acids between the positions 267-325 of the original protein. The resulting new variant contains the active site.

**Accession:** PTI6\_HUMAN

**Name:** PLACENTAL THROMBIN INHIBITOR

15 **Function:** Cytoplasmic antiproteinase

**SEQ ID : 23**

20 **Description:** Deletion of 189 amino acids between the positions 89-278 of the original protein. The resulting new variant contains the active site.

**Accession:** PTI6\_HUMAN

**Name:** PLACENTAL THROMBIN INHIBITOR

**Function:** Cytoplasmic antiproteinase

25

**SEQ ID : 24**

30 **Description:** Replacement of 376 C-terminal amino acids of the original protein by alternative 5 amino acids. The resulting new variant doesn't contain the active site.

**Accession:** IAP2\_HUMAN

**Name:** INHIBITOR OF APOPTOSIS PROTEIN 2

35 **Function:** Apoptotic suppressor. The BIR motifs region interacts with TNF receptor associated factors 1 and 2 (traf1 and traf2) to form an heteromeric complex, which is then recruited to the tumor necrosis factor receptor 2 (TNFR2).

**SEQ ID : 25**

**Description:** Truncated: 305 amino acids compared to 618 aa(protein 2). The  
5 new variant contains exact positions 1-299, last 6 amino acids are different. Two  
SNIPs in positions 235 and 241 of the original protein. The new variant is  
missing Zn Finger and half of 3rd BIR repeat.

**Accession:** SET\_HUMAN  
10 **Name:** PHOSPHATASE 2A INHIBITOR I2PP2A  
**Function:** May be involved in the generation of intracellular signaling  
events that lead to regulation of transcriptional activity after  
binding of a ligand to HLA class II molecules. Potent  
inhibitor of protein phosphatase 2a.

15

**SEQ ID : 26**

**Description:** Extra 83 amino acids in the N-terminus of the protein. The  
added sequence has predicted potential transmembrane domain (probable signal  
20 peptide?)

**Accession:** SET\_HUMAN  
**Name:** PHOSPHATASE 2A INHIBITOR I2PP2A  
**Function:** May be involved in the generation of intracellular signaling  
25 events that lead to regulation of transcriptional activity after  
binding of a ligand to HLA class II molecules. Potent  
inhibitor of protein phosphatase 2a.

**SEQ ID : 27**

30

**Description:** Replacement of 24 C-terminal amino acids of the original  
protein by alternative 8 amino acids. Missing part of ASP/GLU-RICH and  
BREAKPOINT FOR TRANSLOCATION TO FORM SET-CAN  
ONCOGENE.

35

**Accession:** CDNC\_HUMAN  
**Name:** CYCLIN-DEPENDENT KINASE INHIBITOR 1C

- 47 -

**Function:** POTENT TIGHT-BINDING INHIBITOR OF SEVERAL G1 CYCLIN/CDK COMPLEXES (CYCLIN E-CDK2, CYCLIN D2-CDK4, AND CYCLIN A-CDK2) AND, TO LESSER EXTENT, OF THE MITOTIC CYCLIN B-CDC2. NEGATIVE REGULATOR OF CELL PROLIFERATION. MAY PLAY A ROLE IN MAINTENANCE OF THE NONPROLIFERATIVE STATE THROUGHOUT LIFE. SUBCELLULAR LOCATION: NUCLEAR (BY SIMILARITY). DISEASE: CDKN1C MUTATIONS ARE INVOLVED IN TUMOR FORMATION.

**SEQ ID : 28**

**Description:** Deletion of 178 amino acids at the positions 97-275 of the original protein. Insertion of 121 amino acids at the N-terminus. The resulting new variant is missing PAPA repeats.

**Accession:** F13B\_MOUSE

**Name:** COAGULATION FACTOR XIII B CHAIN

**Function:** The B chain of factor XIII is not catalytically active, but is thought to stabilize the a subunits and regulate the rate of transglutaminase formation by thrombin

**SEQ ID : 29****Description**

Deletion of 87 C-terminal amino acids of the original protein. SNIP at position 236 (L->V). The resulting new variant is missing the last shushi repeat.

**Accession:** EGF\_MOUSE

**Name:** PRO-EPIDERMAL GROWTH FACTOR

**Function:** Stimulates the growth of various epidermal and epithelial tissues.

**SEQ ID : 30**

- 48 -

**Description:** Deletion of 641 amino acids between the positions 67-708 of the original protein. Missing 4 EGF-like domains, 2 glycosylations, 9 diSulfide bonds.

5 **Accession:** EGF\_MOUSE  
**Name:** PRO-EPIDERMAL GROWTH FACTOR  
**Function:** Stimulates the growth of various epidermal and epithelial Tissues

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**SEQ ID : 31**

**Description:** Deletion of 641 amino acids between the positions 67-708, and deletion of 45 amino acids between the positions 1020-1065 of the original protein. Missing 4 EGF-like domains, 2 glycosylations, 9 diSulfide bonds. Missing transmembrane domain.

**Accession:** EGF\_MOUSE  
**Name:** PRO-EPIDERMAL GROWTH FACTOR  
**Function:** Stimulates the growth of various epidermal and epithelial tissues

**SEQ ID : 32**

**Description:** Deletion of 641 amino acids between the positions 67-708 of the original protein. Missing 4 EGF-like domains, 2 glycosylations, 9 diSulfide bonds. Replacement of 419 C-terminal amino acids by 5 amino acids.

**Accession:** EGF\_MOUSE  
**Name:** PRO-EPIDERMAL GROWTH FACTOR  
**Function:** Stimulates the growth of various epidermal and epithelial Tissues

**SEQ ID : 33**

**Description:** Deletion of 841 amino acids between the positions 18-859 of the original protein. Missing 5 EGF-like domains and 2 glycosylation sites.

**Accession:** EGF\_MOUSE  
**Name:** PRO-EPIDERMAL GROWTH FACTOR  
**Function:** Stimulates the growth of various epidermal and epithelial Tissues



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**SEQ ID : 34**

**Description:** Deletion of 774 amino acids between the positions 5-779 of the original protein. Missing signal peptide, 5 EGF-like domains, and 2 glycosylation sites.

**Accession:** P53\_MOUSE  
**Name:** CELLULAR TUMOR ANTIGEN P53  
**Function:** Acts as a tumor suppressor in many tumor types. Induces growth arrest or apoptosis depending on the physiological circumstances or cell type, but both activities are involved in tumor suppression.

**SEQ ID : 35**

**Description:** Deletion of 336 N-terminal amino acids of the original protein. Missing ASP/GLU-RICH (ACIDIC), missing hydrophobic domain, missing NUCLEAR LOCALIZATION SIGNAL, missing 1 out of 2 PHOSPHORYLATION sites.

**Accession:** NME3\_HUMAN  
**Name:** GLUTAMATE [NMDA] RECEPTOR SUBUNIT EPSILON 3  
**Function:** NMDA receptor subtype of glutamate-gated ion channels possesses high calcium permeability and voltage-dependent sensitivity to magnesium and is mediated by glycine.

**SEQ ID : 36**

**Description:** Deletion of 381 N-terminal amino acids of the original protein. Missing 2 out of 4 glycosylation sites.

**Accession:** TRFE\_HUMAN  
**Name:** SEROTRANSFERRIN  
**Function:** Iron binding transport proteins

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**SEQ ID : 37**

**Description:** Deletion of 34 amino acids between the positions 654-689 of the original protein. Loss of disulfide bond.

5

**Accession:** TRFE\_HUMAN  
**Name:** SEROTRANSFERRIN  
**Function:** Iron binding transport proteins

10 **SEQ ID : 38**

**Description:** Deletion of 52 amino acids between the positions 447-499 of the original protein. Loss of disulfide bond.

15 **Accession:** BAA23795  
**Name:** Brain ryanodine receptor

**SEQ ID : 39**

20

**Description:** Replacement of 83 C-terminal amino acids from probable cytoplasmic domain of the original protein by alternative 4 amino acids. Resulting in truncated new variant: 4787 compared to 4866, exact 1-4783 with last 4 amino acids different.

25

**Accession:** VIPS\_HUMAN  
**Name:** VASOACTIVE      INTESTINAL      POLYPEPTIDE  
RECEPTOR 2

30

**Function:** This is a receptor for VIP as well as PACAP-38 and -27, the activity of this receptor is mediated by G proteins which activate adenylyl cyclase. Can be coupled to phospholipase C.

**SEQ ID : 40**

35 **Description:** Replacement of 64 C-terminal amino acids of the original protein by alternative 7 amino acids. The resulting new variant is missing the last transmembrane and the cytoplasmic domains.

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**Accession:** PACR\_HUMAN  
**Name:** PITUITARY ADENYLATE CYCLASE ACTIVATING  
POLYPEPTIDE TYPE RECEPTOR

**Function:** This is a receptor for PACAP-27 and PACAP-38. The  
5 activity of this receptor is mediated by G proteins which  
activate adenylyl cyclase. May regulate the release of  
adrenocorticotropin, luteinizing hormone, growth hormone,  
prolactin, epinephrine.

10 **SEQ ID : 41**

**Description:** Deletion of 22 amino acids between the positions 88-110 of the  
original protein. The deletion is in extracellular loop.

15 **Accession:** NRP\_HUMAN  
**Name:** NEUROPILIN VASCULAR ENDOTHELIAL CELL  
GROWTH FACTOR 165 RECEPTOR

**Function:** Calcium-independent cell adhesion molecule that function  
during the formation of certain neuronal circuits. Binds to  
20 semaphorin III and to the VEGF165 isoform of VEGF

**SEQ ID : 42**

**Description:** Deletion of 540 C-terminal amino acids of the original protein,  
25 resulting in truncated new variant (383 compared to 923 amino acids).  
The new variant is missing part of the extracellular domain, the cytoplasmic and  
the transmembrane domains.

**Accession:** NRP\_HUMAN  
30 **Name:** NEUROPILIN VASCULAR ENDOTHELIAL CELL  
GROWTH FACTOR 165 RECEPTOR

**Function:** Calcium-independent cell adhesion molecule that during the  
formation of certain neuronal circuits. Binds to semaphorin  
III and to the VEGF165 isoform of VEGF

35

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**R2\_NV43**

**Description:** Replacement of 595 C-terminal amino acids of the original protein by alternative 11 amino acids. The resulting new variant is truncated (339 compared to 923 amino acids, exact 1-328 with last 11 amino acids different), and is missing part of the extracellular domain, the cytoplasmic and the transmembrane domains.

**Accession:** gi|1899200

**Name:** N-METHYL D-ASPARTATE RECEPTOR SUBTYPE 2A

**Function:** NMDA RECEPTOR SUBTYPE OF GLUTAMATE-GATED ION CHANNELS POSSESSES HIGH CALCIUM PERMEABILITY AND VOLTAGE-DEPENDENT SENSITIVITY TO MAGNESIUM AND IS MEDIATED BY GLYCINE.

SUBUNIT: HETERODIMER OF AN EPSILON SUBUNIT AND A ZETA SUBUNIT.

SUBCELLULAR LOCATION: INTEGRAL MEMBRANE PROTEIN.

SIMILARITY: BELONGS TO THE LIGAND-GATED IONIC CHANNELS FAMILY.

**SEQ ID : 44:**

**Description:** Deletion of 114 amino acids between the positions 1257-1372 of the original protein.

**Accession:** VIPS\_HUMAN

**Name:** VASOACTIVE INTESTINAL POLYPEPTIDE RECEPTOR 2

**Function:** THIS IS A RECEPTOR FOR VIP AS WELL AS PACAP-38 AND -27, THE ACTIVITY OF THIS RECEPTOR IS MEDIATED BY G PROTEINS WHICH ACTIVATE ADENYLYL CYCLASE. CAN BE COUPLED TO PHOSPHOLIPASE C.

SUBCELLULAR LOCATION: INTEGRAL MEMBRANE PROTEIN.

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SIMILARITY: BELONGS TO FAMILY 2 OF  
G-PROTEIN COUPLED RECEPTORS.

**SEQ ID : 45:**

5

**Description:** Replacement of 56 C-terminal amino acids from the  
cytoplasmic domain of the original protein by alternative 73 amino acids.

10 **SEQ ID : 46**

**Description:** Replacement of 56 C-terminal amino acids from the  
cytoplasmic domain of the original protein by alternative 70 amino acids.

15

**Accession:**

IG1R\_HUMAN

**Name:**

INSULIN-LIKE GROWTH FACTOR I RECEPTOR  
PRECURSOR

**Function:**

20

THIS RECEPTOR BINDS INSULIN-LIKE GROWTH  
FACTOR I (IGF I) WITH A HIGH AFFINITY AND IGF II  
WITH A LOWER AFFINITY. IT HAS A  
TYROSINE-PROTEIN KINASE ACTIVITY.

CATALYTIC ACTIVITY: ATP + A PROTEIN TYROSINE  
= ADP + PROTEIN TYROSINE PHOSPHATE.

25

SUBUNIT: TETRAMER OF 2 ALPHA AND 2 BETA  
CHAINS LINKED BY DISULFIDE BONDS. THE ALPHA  
CHAINS

30

CONTRIBUTE TO THE FORMATION OF THE LIGAND-  
BINDING DOMAIN, WHILE THE BETA CHAIN  
CARRIES THE KINASE DOMAIN.

SUBCELLULAR LOCATION: TYPE I MEMBRANE  
PROTEIN.

SIMILARITY: BELONGS TO THE INSULIN RECEPTOR  
FAMILY OF TYROSINE- PROTEIN KINASES.

35

SIMILARITY: CONTAINS 2 FIBRONECTIN TYPE  
III-LIKE DOMAINS.

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**SEQ ID : 47**

**Description:** Deletion of 22 amino acids between the positions 1268-1291 of the original protein. The deleted fragment is part of the cytoplasmic domain of  
5 INSULIN-LIKE GROWTH FACTOR I RECEPTOR, BETA-CHAIN.

**Accession:** NRP\_HUMAN  
**Name:** NEUROPILIN  
10 **Function:** CALCIUM-INDEPENDENT CELL ADHESION  
MOLECULE THAT FUNCTION DURING THE  
FORMATION OF CERTAIN NEURONAL CIRCUITS.  
BINDS TO SEMAPHORIN III AND TO THE VEGF165  
ISOFORM OF VEGF.  
15 SUBCELLULAR LOCATION: TYPE I MEMBRANE  
PROTEIN.  
SIMILARITY: CONTAINS 2 CUB DOMAINS.  
SIMILARITY: CONTAINS 2 F5/8 TYPE C DOMAINS.  
SIMILARITY: CONTAINS 1 MAM DOMAIN.

20

**SEQ ID : 48**

**Description:** Replacement of 282 C-terminal amino acids of the original protein, including the transmembrane domain and the MAM domain, by  
25 alternative 3 amino acids.

**SEQ ID : 49**

**Description:** Deletion of 83 amino acids between the positions 538-622 of  
30 the original protein. The deleted region includes part of the F5/8 TYPE C 2  
domain and part of the MAM domain.

**SEQ ID : 50**

35 **Description:** Deletion of 385 C-terminal amino acids of the original protein, including the transmembrane domain and the MAM domain.

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**Accession:** FGR3\_HUMAN  
**Name:** FIBROBLAST GROWTH FACTOR RECEPTOR 3  
**Function:** SUBCELLULAR LOCATION: TYPE I MEMBRANE  
5 PROTEIN.

DISEASE: DEFECTS IN FGFR3 ARE THE CAUSE OF  
THE AUTOMOSOMAL DOMINANT DISEASE  
ACHONDROPLASIA (ACH); THE MOST FREQUENT  
10 FORM OF SHORT-LIMB DWARFISM. ACH IS  
CHARACTERIZED BY A LONG, NARROW TRUNK,  
SHORT EXTREMITIES, PARTICULARLY IN THE  
PROXIMAL (RHIZOMELIC) SEGMENTS, A LARGE  
HEAD WITH FRONTAL BOSSING, HYPOPLASIA OF  
THE MIDFACE AND A TRIDENT CONFIGURATION  
15 OF THE HANDS.

DISEASE: DEFECTS IN FGFR3 ARE A CAUSE OF  
CROUZON SYNDROME, ALSO CALLED  
CRANIOFACIAL DYSOSTOSIS TYPE I (CFD1).  
CHARACTERIZED BY CRANIOSYNOSTOSIS  
20 (PREMATURE FUSION OF THE SKULL SUTURES),  
HYPERTELORISM, EXOPHTHALMOS AND  
EXTERNAL STRABISMUS, PARROT-BEAKED NOSE,  
SHORT UPPER LIP, HYPOPLASTIC MAXILLA, AND  
A RELATIVE MANDIBULAR PROGNATHISM.

DISEASE: DEFECTS IN FGFR3 ARE A CAUSE OF  
THANATOPHORIC DYSPLASIA (TD) (ALSO KNOWN  
AS THANATOPHORIC DWARFISM), THE MOST  
COMMON NEONATAL LETHAL SKELETAL  
DYSPLASIA, AFFECTED INDIVIDUALS DISPLAY  
30 FEATURES SIMILAR TO THOSE SEEN IN  
HOMOZYGOUS ACHONDROPLASIA. IT CAUSES  
SEVERE SHORTENING OF THE LIMBS WITH  
MACROCEPHALY, NARROW THORAX AND SHORT  
RIBS. IN THE MOST COMMON SUBTYPE (TD1),  
35 FEMUR ARE CURVED, WHILE IN TD2, STRAIGHT  
FEMURS ARE ASSOCIATED WITH CLOVERLEAF  
SKULL.

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5 DISEASE: DEFECTS IN FGFR3 ARE A CAUSE OF  
CRANIOSYNOSTOSIS ADELAIDE TYPE (CRS3), A  
FORM OF CORONAL SYNOSTOSIS (CS)  
CHARACTERIZED BY CRANIOSYNOSTOSIS,  
MIDFACE HYPOPLASIA, DOWNSLANDING  
PALPEBRAL FISSURES, PTOSIS, HIGHLY ARCHED  
PALATE, MID-TO-MODERATE SENSORINEURAL  
HEARING LOSS, NORMAL STATURE,  
BRADYDACTYLY, BROAD BIG TOES.  
10 RADIOLOGICALLY HANDS AND FEET SHOW  
THIMBLE-LIKE MIDDLE PHALANGES, CONED  
EPIPHYSES, AND CARPAL AND TARSAL FUSIONS.  
DISEASE: DEFECTS IN FGFR3 ARE A CAUSE OF THE  
AUTOSOMAL DOMINANT DISEASE HYPO-  
15 CHONDROPLASIA CHARACTERIZED BY  
DISPROPORTIONATE SHORT STATURE. IT  
RESEMBLE ACHONDROPLASIA, BUT WITH A LESS  
SEVERE PHENOTYPE.  
SIMILARITY: BELONGS TO THE FIBROBLAST  
20 GROWTH FACTOR RECEPTOR FAMILY.  
SIMILARITY: CONTAINS 3 IMMUNOGLOBULIN-  
LIKE DOMAINS.

**SEQ ID : 51**

25 **Description:** Replacement of 496 C-terminal amino acids of the original  
protein by alternative 79 amino acids.. The deleted region includes the C-terminal  
part of the extracellular domain, the transmembrane domain, the cytoplasmic  
domain, the protein kinase domain and the two ATP binding domains.

30

**EGF MOUSE****EPIDERMAL GROWTH FACTOR**

35

FUNCTION: THE GROWTH FACTOR STIMULATES THE GROWTH OF  
VARIOUS EPIDERMAL AND EPITHELIAL TISSUES IN VIVO AND IN  
VITRO AND OF SOME FIBROBLASTS IN CELL CULTURE.  
SUBCELLULAR LOCATION: TYPE I MEMBRANE PROTEIN.



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SIMILARITY: CONTAINS 8 COMPLETE AND ONE INCOMPLETE EGF-LIKE DOMAINS.

**SEQ ID NO : 52**

5

Deletion of 144 amino acids between the positions 1020-1165, including the transmembrane domain and part of the cytoplasmic domain of the original protein.

10 **SEQ ID NO : 53**

Replacement of 418 C-terminal amino acids of the original protein by alternative 5 amino acids. The deleted region includes the EGF active chain, 4 out of 9 EGF-like domains within the extracellular region of the protein, the  
15 transmembrane and the cytoplasmic regions.

**SEQ ID NO : 54**

Deletion of 641 amino acids between the positions 66-707 of the original protein.  
20 The deleted region is in the extracellular part of the protein and it includes 4 out of 9 EGF-like domains. NV-20 contains the original signal peptide, part of the extracellular domain, the epidermal growth factor chain (located between the positions 977-1029 of the original protein), and the original transmembrane and the cytoplasmic domains.

25

**SEQ ID NO : 55**

Deletion of 842 amino acids between the positions 17-859 of the original protein  
30 (including replacement of the amino acid in the position 859 by an alternative one). The deleted region is in the extracellular part of the protein and it includes 5 out of 9 EGF-like domains. NV-20 contains the original signal peptide, part of the extracellular domain, the epidermal growth factor chain (located between the positions 977-1029 of the original protein), and the original transmembrane and  
35 the cytoplasmic domains.

**ACE\_MOUSE**

40

**ANGIOTENSIN-CONVERTING ENZYME**

- FUNCTION: CONVERTS ANGIOTENSIN I TO ANGIOTENSIN II BY RELEASE OF THE TERMINAL HIS-LEU, THIS RESULTS IN AN INCREASE OF THE VASOCONSTRICTOR ACTIVITY OF ANGIOTENSIN.
- 5 CATALYTIC ACTIVITY: RELEASE OF A C-TERMINAL DIPEPTIDE, OLIGOPEPTIDE-|-XAA-XBB, WHEN XAA IS NOT PRO, AND XBB IS NEITHER ASP NOR GLU. CONVERTS ANGIOTENSIN I TO ANGIOTENSIN II.
- 10 COFACTOR: BINDS TWO ZINC IONS (BY SIMILARITY).  
SUBCELLULAR LOCATION: TYPE I MEMBRANE PROTEIN.  
ALTERNATIVE PRODUCTS: THE TESTICULAR ANGIOTENSIN-CONVERTING ENZYME IS TRANSCRIBED FROM THE SAME GENE AS THE SOMATIC ISOFORM, PROBABLY FROM AN ALTERNATIVE START
- 15 SITE.  
SIMILARITY: BELONGS TO PEPTIDASE FAMILY M2 (ZINC METALLOPROTEASE).

20 **SEQ ID NO : 56**

Replacement of 77 C-terminal amino acids of the original protein, including the entire transmembrane and cytoplasmic domains, by alternative 14 amino acids.

25

**ESR1\_MOUSE**

**ESTROGEN RECEPTOR**

- 30 FUNCTION: THE STEROID HORMONES AND THEIR RECEPTORS ARE INVOLVED IN THE REGULATION OF EUKARYOTIC GENE EXPRESSION AND AFFECT CELLULAR PROLIFERATION AND DIFFERENTIATION IN TARGET TISSUES.  
SUBUNIT: HOMODIMER.
- 35 SUBCELLULAR LOCATION: NUCLEAR.  
DOMAIN: COMPOSED OF THREE DOMAINS: A MODULATING N-TERMINAL DOMAIN, A DNA-BINDING DOMAIN AND A C-TERMINAL STEROID-BINDING DOMAIN.  
MISCELLANEOUS: IN THE ABSENCE OF LIGAND, STEROID HORMONE
- 40 RECEPTORS ARE THOUGHT TO BE WEAKLY ASSOCIATED WITH NUCLEAR COMPONENTS; HORMONE BINDING GREATLY INCREASES RECEPTOR AFFINITY. THE HORMONE-RECEPTOR COMPLEX APPEARS TO RECOGNIZE DISCRETE DNA SEQUENCES UPSTREAM OF TRANSCRIPTIONAL START SITES.

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SIMILARITY: BELONGS TO THE NUCLEAR HORMONE RECEPTORS  
FAMILY. NR3 SUBFAMILY.

**SEQ ID : 57**

5

Replacement of 229 C-terminal amino acids of the original protein, including part of the steroid-binding domain, by an alternative 12 amino acids.

10

**FA7\_MOUSE****COAGULATION FACTOR VII PRECURSOR**

15 FUNCTION: CIRCULATES IN THE BLOOD IN A ZYMOGEN FORM.  
FACTOR VII IS CONVERTED TO FACTOR VIIA BY FACTOR XA,  
FACTOR XIIA, FACTOR IXA, OR THROMBIN BY MINOR PROTEOLYSIS.  
IN THE PRESENCE OF TISSUE FACTOR AND CALCIUM IONS, FACTOR  
VIIA THEN CONVERTS FACTOR X TO FACTOR XA BY LIMITED  
20 PROTEOLYSIS. FACTOR VIIA WILL ALSO CONVERT FACTOR IX TO  
FACTOR IXA IN THE PRESENCE OF TISSUE FACTOR AND CALCIUM  
(BY SIMILARITY).

CATALYTIC ACTIVITY: HYDROLYSES ONE ARG-|-ILE BOND IN  
FACTOR X TO FORM FACTOR XA.

25 SUBUNIT: HETERODIMER OF A LIGHT CHAIN AND A HEAVY CHAIN  
LINKED BY A DISULFIDE BOND (BY SIMILARITY).

TISSUE SPECIFICITY: PLASMA.

PTM: THE VITAMIN K-DEPENDENT, ENZYMATIC CARBOXYLATION  
OF SOME GLUTAMIC ACID RESIDUES ALLOWS THE MODIFIED  
30 PROTEIN TO BIND CALCIUM (BY SIMILARITY).

SIMILARITY: CONTAINS 2 EGF-LIKE DOMAINS.

SIMILARITY: BELONGS TO PEPTIDASE FAMILY S1; ALSO KNOWN AS  
THE TRYPSIN FAMILY.

**35 SEQ ID : 58**

Deletion of 101 amino acids, between the positions 119-220 of the original  
protein. The deleted region contains 74 amino acids from the C-terminal end of  
the factor VII light chain, and 26 amino acids from the N-terminal end of the  
40 factor VII heavy catalytic chain. The deleted region includes EGF-like 2 domain  
and the cleavage site (by factor XA, factor XIIA, factor IXA, or thrombin) of

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the original protein.

## CAL0\_MOUSE

5

### CALCITONIN PRECURSOR

FUNCTION: CAUSES A RAPID BUT SHORT-LIVED DROP IN THE LEVEL  
OF CALCIUM AND PHOSPHATE IN BLOOD BY PROMOTING THE  
INCORPORATION OF THOSE IONS IN THE BONES.

10 ALTERNATIVE PRODUCTS: THE CALCITONIN PRECURSOR AND THE  
CALCITONIN RELATED PEPTIDE PRECURSOR ARE OBTAINED BY  
TISSUE-SPECIFIC SPLICING OF THE SAME GENE.  
SIMILARITY: BELONGS TO THE CALCITONIN FAMILY.

15

SEQ ID NO : 59

Deletion of 33 amino acids, spanning the positions 18-50, between the signal and  
the calcitonin peptide in the original precursor protein.

20

gi 2826776

## VESICULAR INHIBITORY AMINO ACID TRANSPORTER

25

function="uptake of GABA and glycine into synaptic vesicles"

SEQ ID NO : 60

30

Replacement of the last 7 C-terminal amino acids of the original protein by  
alternative 11 amino acids.

35

## PTI6\_HUMAN

### PLACENTAL THROMBIN INHIBITOR

40 CYTOPLASMIC ANTIPROTEINASE, PROTEASE INHIBITOR 6.  
SIMILARITY: BELONGS TO THE SERPIN FAMILY. OV-SERPIN  
SUBFAMILY.

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**SEQ ID NO : 61**

Replacement of the last 4 C-terminal amino acids of the original protein by alternative 28 amino acids.

5

**SEQ ID NO : 62**

Replacement of the last 16 C-terminal amino acids of the original protein by alternative 12 amino acids.

10

**RIN1\_HUMAN**

15

**RAS INTERACTION/INTERFERENCE PROTEIN 1**  
**(RAS INHIBITOR JC99)**  
**(FRAGMENT)**

**SEQ ID NO : 63**

20

Replacement of 158 last C-terminal amino acids of the original protein by alternative 71 amino acids with probable transmembrane region.

25

**CDNC\_HUMAN****CYCLIN-DEPENDENT KINASE INHIBITOR 1C P57**

30 FUNCTION: POTENT TIGHT-BINDING INHIBITOR OF SEVERAL G1 CYCLIN/CDK COMPLEXES (CYCLIN E-CDK2, CYCLIN D2-CDK4, AND CYCLIN A-CDK2) AND, TO LESSER EXTENT, OF THE MITOTIC CYCLIN B-CDC2. NEGATIVE REGULATOR OF CELL PROLIFERATION. MAY PLAY A ROLE IN MAINTENANCE OF THE NONPROLIFERATIVE STATE

35

THROUGHOUT LIFE.  
SUBCELLULAR LOCATION: NUCLEAR (BY SIMILARITY).

DISEASE: CDKN1C MUTATIONS ARE INVOLVED IN TUMOR FORMATION.

40

**SEQ ID NO : 64**

Addition of 121 amino acids at the N-terminus of the protein.

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**CDN2\_HUMAN**

5       **CYCLIN-DEPENDENT KINASE 4 INHIBITOR A (CDK4I)**  
          **(MULTIPLE TUMOR SUPPRESSOR 1) (MTS1)**

10       FUNCTION: INTERACTS STRONGLY WITH CDK4 AND CDK6. INHIBITS  
          ITS ABILITY TO INTERACT WITH CYCLINS D. COULD ACT AS A  
          NEGATIVE REGULATOR OF THE PROLIFERATION OF NORMAL  
          CELLS.

          SUBUNIT: HETERODIMER WITH CDK4 OR CDK6.

15       DISEASE: CDKN2A MUTATIONS ARE INVOLVED IN TUMOR  
          FORMATION IN A WIDE RANGE OF TISSUES.

          SIMILARITY: BELONGS TO THE CDKN2 FAMILY OF  
          CYCLIN-DEPENDENT KINASE INHIBITORS.

          SIMILARITY: CONTAINS 4 ANK REPEATS.

20       **SEQ ID NO : 65**

          Replacement of 5 amino acids at the positions 18, 24, 27, 30, 37 of the original  
          protein by alternative amino acids. Replacement of last 4 C-terminal amino acids  
25       of the original protein by alternative 20 amino acids.

**CDN5\_HUMAN**

30       **CYCLIN-DEPENDENT KINASE 4 INHIBITOR B**  
          **(MULTIPLE TUMOR SUPPRESSOR 2)**

          FUNCTION: INTERACTS STRONGLY WITH CDK4 AND CDK6. POTENT  
          INHIBITOR. POTENTIAL EFFECTOR OF TGF-BETA INDUCED CELL  
35       CYCLE ARREST.

          SUBUNIT: HETERODIMER OF P14 WITH CDK4.

          DISEASE: CDKN2B MUTATIONS ARE INVOLVED IN TUMOR  
          FORMATION.

          SIMILARITY: BELONGS TO THE CDKN2 FAMILY OF  
40       CYCLIN-DEPENDENT KINASE INHIBITORS.

          SIMILARITY: CONTAINS 2 ANK REPEATS.

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SEQ ID NO : 66

Replacement of the last 6 C-terminal amino acids of the original protein by alternative 52 amino acids.

5

**HEP2\_HUMAN****HEPARIN COFACTOR II PRECURSOR**  
**PROTEASE INHIBITOR LEUSERPIN 2**

10

FUNCTION: THROMBIN INHIBITOR ACTIVATED BY THE GLYCOSAMINOGLYCANS, HEPARIN OR DERMATAN SULFATE. IN THE PRESENCE OF THE LATTER, HC-II BECOMES THE PREDOMINANT THROMBIN INHIBITOR IN PLACE OF ANTITHROMBIN III (AT). ALSO INHIBITS CHYMOTRYPSIN, BUT IN A GLYCOSAMINOGLYCAN-INDEPENDENT MANNER.

15

FUNCTION: PEPTIDES AT THE N-TERMINAL OF HC-II HAVE CHEMOTACTIC ACTIVITY FOR BOTH MONOCYTES AND NEUTROPHILS.

20

TISSUE SPECIFICITY: EXPRESSED PREDOMINANTLY IN LIVER.

DOMAIN: THE N-TERMINAL ACIDIC REPEAT REGION MEDIATES, IN PART, THE

GLYCOSAMINOGLYCAN-ACCELERATED THROMBIN INHIBITION.

DISEASE: DEFECTS IN HCF2 ARE ASSOCIATED WITH THROMBOSIS (THROMBOPHILIA).

25

SIMILARITY: BELONGS TO THE SERPIN FAMILY.

SEQ ID NO : 67

30 Deletion of 150 amino acids, between the positions 334-485, of the original protein. The deleted region includes the reactive bond (the active site) of the original protein. NV-33 does contain the chemotactic activity domain, the glycosaminoglycan-binding site and the hirudin-like 2 x 11 AA approximate repeats, Asp/Glu rich.

35

**TFP2\_HUMAN****TISSUE FACTOR PATHWAY INHIBITOR 2 PRECURSOR**

40

FUNCTION: SEEMS TO INHIBIT TRYPSIN, FACTOR VII(A)/TISSUE FACTOR, WEAKLY FACTOR XA. HAS NO EFFECT ON THROMBIN.

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DOMAIN: THIS INHIBITOR CONTAINS THREE INHIBITORY DOMAINS.  
SIMILARITY: BELONGS TO THE BPTI/KUNITZ FAMILY OF  
INHIBITORS. HIGHLY SIMILAR TO TPFI.

5 **SEQ ID NO : 68**

Replacement of 36 C-terminal amino acids of the original protein by alternative  
12 amino acids. The deleted region includes part of the BPTI/KUNITZ inhibitor  
domain-3 and the poly-Lysine domain of the original protein.

10

**SEQ ID NO : 69**

Deletion of 25 amino acids, between the positions 153-178 of the original  
15 protein, and replacement of the amino acid at the position 179 by alternative one.  
The deleted region includes the active site and part of the BPTI/KUNITZ  
inhibitor domain-3.

20

**TFPI\_HUMAN**

**TISSUE FACTOR PATHWAY INHIBITOR PRECURSOR (TFPI)**

25 **SEQ ID NO : 70**

Replacement of 95 C-terminal amino acids of the original protein, containing the  
entire BPTI/KUNITZ inhibitor-3 domain, by alternative 16 amino acids.

30

**Example II: Variant nucleic acid sequence**

The nucleic acid sequences of the invention include nucleic acid  
sequences which encode variant product and fragments and analogs thereof. The  
nucleic acid sequences may alternatively be sequences complementary to the  
35 above coding sequence, or to a region of said coding sequence. The length of the  
complementary sequence is sufficient to avoid the expression of the coding  
sequence. The nucleic acid sequences may be in the form of RNA or in the form  
of DNA, and include messenger RNA, synthetic RNA and DNA, cDNA, and  
genomic DNA. The DNA may be double-stranded or single-stranded, and if



single-stranded may be the coding strand or the non-coding (anti-sense, complementary) strand. The nucleic acid sequences may also both include dNTPs, rNTPs as well as non naturally occurring sequences. The sequence may also be a part of a hybrid between an amino acid sequence and a nucleic acid  
5 sequence.

In a general embodiment, the nucleic acid sequence has at least 90%, identity with any one of the sequence identified as SEQ ID NO: 1 to SEQ ID NO: 174 provided that this sequence is not completely identical with that of the original sequence.

10 The nucleic acid sequences may include the coding sequence by itself. By another alternative the coding region may be in combination with additional coding sequences, such as those coding for fusion protein or signal peptides, in combination with non-coding sequences, such as introns and control elements, promoter and terminator elements or 5' and/or 3' untranslated regions, effective  
15 for expression of the coding sequence in a suitable host, and/or in a vector or host environment in which the variant nucleic acid sequence is introduced as a heterologous sequence.

The nucleic acid sequences of the present invention may also have the product coding sequence fused in-frame to a marker sequence which allows for  
20 purification of the variant product. The marker sequence may be, for example, a hexahistidine tag to provide for purification of the mature polypeptide fused to the marker in the case of a bacterial host, or, the marker sequence may be a hemagglutinin (HA) tag when a mammalian host, e.g. COS-7 cells, is used. The HA tag corresponds to an epitope derived from the influenza hemagglutinin  
25 protein (Wilson, I., *et al. Cell* 37:767 (1984)).

Also included in the scope of the invention are fragments as defined above also referred to herein as oligonucleotides, typically having at least 20 bases, preferably 20-30 bases corresponding to a region of the coding-sequence nucleic acid sequence. The fragments may be used as probes, primers, and when

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complementary also as antisense agents, and the like, according to known methods.

As indicated above, the nucleic acid sequence may be substantially a depicted in any one of SEQ ID NO: 1 to SEQ ID NO: 87 or fragments thereof or  
5 sequences having at least 90% identity to the above sequence as explained above. Alternatively, due to the degenerative nature of the genetic code, the sequence may be a sequence coding for any one of the amino acid sequence of SEQ ID NO: 88 to SEQ ID NO: 174, or fragments or analogs of said amino acid sequence.

10

#### A. Preparation of nucleic acid sequences

The nucleic acid sequences may be obtained by screening cDNA libraries using oligonucleotide probes which can hybridize to or PCR-amplify nucleic acid sequences which encode the variant products disclosed above. cDNA libraries  
15 prepared from a variety of tissues are commercially available and procedures for screening and isolating cDNA clones are well-known to those of skill in the art. Such techniques are described in, for example, Sambrook *et al.* (1989) Molecular Cloning: A Laboratory Manual (2nd Edition), Cold Spring Harbor Press, Plainview, N.Y. and Ausubel FM *et al.* (1989) Current Protocols in Molecular  
20 Biology, John Wiley & Sons, New York, N.Y.

The nucleic acid sequences may be extended to obtain upstream and downstream sequences such as promoters, regulatory elements, and 5' and 3' untranslated regions (UTRs). Extension of the available transcript sequence may be performed by numerous methods known to those of skill in the art, such as  
25 PCR or primer extension (Sambrook *et al.*, *supra*), or by the RACE method using, for example, the Marathon RACE kit (Clontech, Cat. # K1802-1).

Alternatively, the technique of "restriction-site" PCR (Gobinda *et al.* *PCR Methods Applic.* 2:318-22, (1993)), which uses universal primers to retrieve flanking sequence adjacent a known locus, may be employed. First, genomic  
30 DNA is amplified in the presence of primer to a linker sequence and a primer

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specific to the known region. The amplified sequences are subjected to a second round of PCR with the same linker primer and another specific primer internal to the first one. Products of each round of PCR are transcribed with an appropriate RNA polymerase and sequenced using reverse transcriptase.

5 Inverse PCR can be used to amplify or extend sequences using divergent primers based on a known region (Triglia, T. *et al.*, *Nucleic Acids Res.* 16:8186, (1988)). The primers may be designed using OLIGO(R) 4.06 Primer Analysis Software (1992; National Biosciences Inc, Plymouth, Minn.), or another appropriate program, to be 22-30 nucleotides in length, to have a GC content of  
10 50% or more, and to anneal to the target sequence at temperatures about 68-72°C.

The method uses several restriction enzymes to generate a suitable fragment in the known region of a gene. The fragment is then circularized by intramolecular ligation and used as a PCR template.

Capture PCR (Lagerstrom, M. *et al.*, *PCR Methods Applic.* 1:111-19, (1991)) is a method for PCR amplification of DNA fragments adjacent to a  
15 known sequence in human and yeast artificial chromosome DNA. Capture PCR also requires multiple restriction enzyme digestions and ligations to place an engineered double-stranded sequence into a flanking part of the DNA molecule before PCR.

20 Another method which may be used to retrieve flanking sequences is that of Parker, J.D., *et al.*, *Nucleic Acids Res.*, 19:3055-60, (1991)). Additionally, one can use PCR, nested primers and PromoterFinder™ libraries to "walk in" genomic DNA (PromoterFinder™; Clontech, Palo Alto, CA). This process avoids the need to screen libraries and is useful in finding intron/exon junctions. Preferred  
25 libraries for screening for full length cDNAs are ones that have been size-selected to include larger cDNAs. Also, random primed libraries are preferred in that they will contain more sequences which contain the 5' and upstream regions of genes.

A randomly primed library may be particularly useful if an oligo d(T) library does not yield a full-length cDNA. Genomic libraries are useful for  
30 extension into the 5' nontranslated regulatory region.

The nucleic acid sequences and oligonucleotides of the invention can also be prepared by solid-phase methods, according to known synthetic methods. Typically, fragments of up to about 100 bases are individually synthesized, then joined to form continuous sequences up to several hundred bases.

5

**B. Use of variant nucleic acid sequence for the production of variant products**

In accordance with the present invention, nucleic acid sequences specified  
10 above may be used as recombinant DNA molecules that direct the expression of variant products.

As will be understood by those of skill in the art, it may be advantageous to produce variant product-encoding nucleotide sequences possessing codons other than those which appear in any one of SEQ ID NO: 1 to SEQ ID NO: 87  
15 which are those which naturally occur in the human genome. Codons preferred by a particular prokaryotic or eukaryotic host (Murray, E. *et al. Nuc Acids Res.*, 17:477-508, (1989)) can be selected, for example, to increase the rate of variant product expression or to produce recombinant RNA transcripts having desirable properties, such as a longer half-life, than transcripts produced from naturally  
20 occurring sequence.

The nucleic acid sequences of the present invention can be engineered in order to alter a variant product coding sequence for a variety of reasons, including but not limited to, alterations which modify the cloning, processing and/or expression of the product. For example, alterations may be introduced  
25 using techniques which are well known in the art, e.g., site-directed mutagenesis, to insert new restriction sites, to alter glycosylation patterns, to change codon preference, etc.

The present invention also includes recombinant constructs comprising one or more of the sequences as broadly described above. The constructs  
30 comprise a vector, such as a plasmid or viral vector, into which a nucleic acid sequence of the invention has been inserted, in a forward or reverse orientation.

In a preferred aspect of this embodiment, the construct further comprises regulatory sequences, including, for example, a promoter, operably linked to the sequence. Large numbers of suitable vectors and promoters are known to those of skill in the art, and are commercially available. Appropriate cloning and  
5 expression vectors for use with prokaryotic and eukaryotic hosts are also described in Sambrook, *et al.*, (*supra*).

The present invention also relates to host cells which are genetically engineered with vectors of the invention, and the production of the product of the invention by recombinant techniques. Host cells are genetically engineered (i.e.,  
10 transduced, transformed or transfected) with the vectors of this invention which may be, for example, a cloning vector or an expression vector. The vector may be, for example, in the form of a plasmid, a viral particle, a phage, etc. The engineered host cells can be cultured in conventional nutrient media modified as appropriate for activating promoters, selecting transformants or amplifying the  
15 expression of the variant nucleic acid sequence. The culture conditions, such as temperature, pH and the like, are those previously used with the host cell selected for expression, and will be apparent to those skilled in the art.

The nucleic acid sequences of the present invention may be included in any one of a variety of expression vectors for expressing a product. Such vectors  
20 include chromosomal, nonchromosomal and synthetic DNA sequences, e.g., derivatives of SV40; bacterial plasmids; phage DNA; baculovirus; yeast plasmids; vectors derived from combinations of plasmids and phage DNA, viral DNA such as vaccinia, adenovirus, fowl pox virus, and pseudorabies. However, any other vector may be used as long as it is replicable and viable in the host.  
25 The appropriate DNA sequence may be inserted into the vector by a variety of procedures. In general, the DNA sequence is inserted into an appropriate restriction endonuclease site(s) by procedures known in the art. Such procedures and related sub-cloning procedures are deemed to be within the scope of those skilled in the art.

The DNA sequence in the expression vector is operatively linked to an appropriate transcription control sequence (promoter) to direct mRNA synthesis. Examples of such promoters include: LTR or SV40 promoter, the *E.coli lac* or *trp* promoter, the phage lambda *PL* promoter, and other promoters known to control expression of genes in prokaryotic or eukaryotic cells or their viruses. The expression vector also contains a ribosome binding site for translation initiation, and a transcription terminator. The vector may also include appropriate sequences for amplifying expression. In addition, the expression vectors preferably contain one or more selectable marker genes to provide a phenotypic trait for selection of transformed host cells such as dihydrofolate reductase or neomycin resistance for eukaryotic cell culture, or such as tetracycline or ampicillin resistance in *E.coli*.

The vector containing the appropriate DNA sequence as described above, as well as an appropriate promoter or control sequence, may be employed to transform an appropriate host to permit the host to express the protein. Examples of appropriate expression hosts include: bacterial cells, such as *E.coli*, *Streptomyces*, *Salmonella typhimurium*; fungal cells, such as yeast; insect cells such as *Drosophila* and *Spodoptera Sf9*; animal cells such as CHO, COS, HEK 293 or Bowes melanoma; adenoviruses; plant cells, etc. The selection of an appropriate host is deemed to be within the scope of those skilled in the art from the teachings herein. The invention is not limited by the host cells employed.

In bacterial systems, a number of expression vectors may be selected depending upon the use intended for the variant product. For example, when large quantities of variant product are needed for the induction of antibodies, vectors which direct high level expression of fusion proteins that are readily purified may be desirable. Such vectors include, but are not limited to, multifunctional *E.coli* cloning and expression vectors such as *Bluescript*(R) (Stratagene), in which the variant polypeptide coding sequence may be ligated into the vector in-frame with sequences for the amino-terminal Met and the subsequent 7 residues of beta-galactosidase so that a hybrid protein is produced;

*pIN* vectors (Van Heeke & Schuster *J. Biol. Chem.* **264**:5503-5509, (1989)); *pET* vectors (Novagen, Madison WI); and the like.

In the yeast *Saccharomyces cerevisiae* a number of vectors containing constitutive or inducible promoters such as alpha factor, alcohol oxidase and  
5 PGH may be used. For reviews, see Ausubel *et al.* (*supra*) and Grant *et al.*, (*Methods in Enzymology* **153**:516-544, (1987)).

In cases where plant expression vectors are used, the expression of a sequence encoding variant product may be driven by any of a number of promoters. For example, viral promoters such as the 35S and 19S promoters of  
10 *CaMV* (Brisson *et al.*, *Nature* **310**:511-514, (1984)) may be used alone or in combination with the omega leader sequence from TMV (Takamatsu *et al.*, *EMBO J.*, **6**:307-311, (1987)). Alternatively, plant promoters such as the small subunit of RUBISCO (Coruzzi *et al.*, *EMBO J.* **3**:1671-1680, (1984); Broglie *et al.*, *Science* **224**:838-843, (1984)); or heat shock promoters (Winter J and  
15 Sinibaldi R.M., *Results Probl. Cell Differ.*, **17**:85-105, (1991)) may be used. These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. For reviews of such techniques, see Hobbs S. or Murry L.E. (1992) in McGraw Hill Yearbook of Science and Technology, McGraw Hill, New York, N.Y., pp 191-196; or Weissbach and Weissbach (1988)  
20 *Methods for Plant Molecular Biology*, Academic Press, New York, N.Y., pp 421-463.

Variant product may also be expressed in an insect system. In one such system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes in *Spodoptera frugiperda* cells or in *Trichoplusia*  
25 larvae. The variant product coding sequence may be cloned into a nonessential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of variant coding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat protein coat. The recombinant viruses are then used to infect *S. frugiperda* cells or

*Trichoplusia* larvae in which variant protein is expressed (Smith *et al.*, *J. Virol.* 46:584, (1983); Engelhard, E.K. *et al.*, *Proc. Nat. Acad. Sci.* 91:3224-7, (1994)).

In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, a  
5 variant product coding sequence may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a nonessential E1 or E3 region of the viral genome will result in a viable virus capable of expressing variant protein in infected host cells (Logan and Shenk, *Proc. Natl. Acad. Sci.* 81:3655-59, (1984). In addition,  
10 transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be required for efficient translation of a variant product coding sequence. These signals include the ATG initiation codon and adjacent sequences. In cases where variant product coding sequence,  
15 its initiation codon and upstream sequences are inserted into the appropriate expression vector, no additional translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous transcriptional control signals including the ATG initiation codon must be provided. Furthermore, the initiation codon must be in the correct  
20 reading frame to ensure transcription of the entire insert. Exogenous transcriptional elements and initiation codons can be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers appropriate to the cell system in use (Scharf, D. *et al.*, (1994) *Results Probl. Cell Differ.*, 20:125-62, (1994); Bittner *et al.*, *Methods in*  
25 *Enzymol* 153:516-544, (1987)).

In a further embodiment, the present invention relates to host cells containing the above-described constructs. The host cell can be a higher eukaryotic cell, such as a mammalian cell, or a lower eukaryotic cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell.  
30 Introduction of the construct into the host cell can be effected by calcium



phosphate transfection, DEAE-Dextran mediated transfection, or electroporation (Davis, L., Dibner, M., and Battey, I. (1986) Basic Methods in Molecular Biology). Cell-free translation systems can also be employed to produce polypeptides using RNAs derived from the DNA constructs of the present  
5 invention.

A host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the protein include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation and  
10 acylation. Post-translational processing which cleaves a "*pre-pro*" form of the protein may also be important for correct insertion, folding and/or function. Different host cells such as CHO, HeLa, MDCK, 293, WI38, etc. have specific cellular machinery and characteristic mechanisms for such post-translational activities and may be chosen to ensure the correct modification and processing of  
15 the introduced, foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express variant product may be transformed using expression vectors which contain viral origins of replication or endogenous expression elements and a selectable marker gene.  
20 Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which successfully express the introduced sequences. Resistant clumps of stably transformed cells can be  
25 proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler M., *et al.*, *Cell* 11:223-32, (1977)) and adenine phosphoribosyltransferase (Lowy I., *et al.*, *Cell* 22:817-23, (1980)) genes which  
30 can be employed in *tk*- or *aprt*- cells, respectively. Also, antimetabolite,

antibiotic or herbicide resistance can be used as the basis for selection; for example, *dhfr* which confers resistance to methotrexate (Wigler M., *et al.*, *Proc. Natl. Acad. Sci.* 77:3567-70, (1980)); *npt*, which confers resistance to the aminoglycosides neomycin and G-418 (Colbere-Garapin, F. *et al.*, *J. Mol. Biol.*,  
5 150:1-14, (1981)) and *als* or *pat*, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, *trpB*, which allows cells to utilize indole in place of tryptophan, or *hisD*, which allows cells to utilize histinol in place of histidine (Hartman S.C. and R.C. Mulligan, *Proc. Natl. Acad. Sci.*  
10 85:8047-51, (1988)). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate, GUS, and luciferase and its substrates, luciferin and ATP, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C.A. *et al.*,  
15 *Methods Mol. Biol.*, 55:121-131, (1995)).

Host cells transformed with a nucleotide sequence encoding variant product may be cultured under conditions suitable for the expression and recovery of the encoded protein from cell culture. The product produced by a recombinant cell may be secreted or contained intracellularly depending on the  
20 sequence and/or the vector used. As will be understood by those of skill in the art, expression vectors containing nucleic acid sequences encoding variant product can be designed with signal sequences which direct secretion of variant product through a prokaryotic or eukaryotic cell membrane.

The variant product may also be expressed as a recombinant protein with  
25 one or more additional polypeptide domains added to facilitate protein purification. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS  
30 extension/affinity purification system (Immunex Corp, Seattle, Wash.). The

inclusion of a protease-cleavable polypeptide linker sequence between the purification domain and variant product is useful to facilitate purification. One such expression vector provides for expression of a fusion protein comprising a variant polypeptide fused to a polyhistidine region separated by an enterokinase  
5 cleavage site. The histidine residues facilitate purification on IMLAC (immobilized metal ion affinity chromatography, as described in Porath, *et al.*, *Protein Expression and Purification*, 3:263-281, (1992)) while the enterokinase cleavage site provides a means for isolating variant polypeptide from the fusion protein. *pGEX* vectors (Promega, Madison, Wis.) may also be used to express  
10 foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption to ligand-agarose beads (e.g., glutathione-agarose in the case of GST-fusions) followed by elution in the presence of free ligand.

Following transformation of a suitable host strain and growth of the host  
15 strain to an appropriate cell density, the selected promoter is induced by appropriate means (e.g., temperature shift or chemical induction) and cells are cultured for an additional period. Cells are typically harvested by centrifugation, disrupted by physical or chemical means, and the resulting crude extract retained for further purification. Microbial cells employed in expression of proteins can  
20 be disrupted by any convenient method, including freeze-thaw cycling, sonication, mechanical disruption, or use of cell lysing agents, or other methods, which are well known to those skilled in the art.

The variant products can be recovered and purified from recombinant cell cultures by any of a number of methods well known in the art, including  
25 ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography, and lectin chromatography. Protein refolding steps can be used, as necessary, in completing configuration of the mature protein. Finally, high

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performance liquid chromatography (HPLC) can be employed for final purification steps.

### C. Diagnostic applications utilizing nucleic acid sequences

5 The nucleic acid sequences of the present invention may be used for a variety of diagnostic purposes. The nucleic acid sequences may be used to detect and quantitate expression of the variant in patient's cells, e.g. biopsied tissues, by detecting the presence of mRNA coding for variant product. Alternatively, the assay may be used to detect soluble variant in the serum or blood. This assay  
10 typically involves obtaining total mRNA from the tissue or serum and contacting the mRNA with a nucleic acid probe. The probe is a nucleic acid molecule of at least 20 nucleotides, preferably 20-30 nucleotides, capable of specifically hybridizing with a sequence included within the sequence of a nucleic acid molecule encoding variant product under hybridizing conditions, detecting the  
15 presence of mRNA hybridized to the probe, and thereby detecting the expression of variant. This assay can be used to distinguish between absence, presence, and excess expression of variant product and to monitor levels of variant expression during therapeutic intervention. In addition, the assay may be used to compare the levels of the variant of the invention to the levels of the original sequence from  
20 which it has been varied or to levels of other variants, which comparison may have some physiological meaning.

The invention also contemplates the use of the nucleic acid sequences as a diagnostic for diseases resulting from inherited defective variant sequences, or diseases in which the ratio of the amount of the original sequence from which the  
25 variant was varied to the novel variants of the invention is altered. These sequences can be detected by comparing the sequences of the defective (i.e., mutant) variant coding region with that of a normal coding region. Association of the sequence coding for mutant variant product with abnormal variant product activity may be verified. In addition, sequences encoding mutant variant products  
30 can be inserted into a suitable vector for expression in a functional assay system

(e.g., colorimetric assay, complementation experiments in a variant protein deficient strain of HEK293 cells) as yet another means to verify or identify mutations. Once mutant genes have been identified, one can then screen populations of interest for carriers of the mutant gene.

5 Individuals carrying mutations in the nucleic acid sequence of the present invention may be detected at the DNA level by a variety of techniques. Nucleic acids used for diagnosis may be obtained from a patient's cells, including but not limited to such as from blood, urine, saliva, placenta, tissue biopsy and autopsy material. Genomic DNA may be used directly for detection or may be amplified  
10 enzymatically by using PCR (Saiki, *et al.*, *Nature* 324:163-166, (1986)) prior to analysis. RNA or cDNA may also be used for the same purpose. As an example, PCR primers complementary to the nucleic acid of the present invention can be used to identify and analyze mutations in the gene of the present invention. Deletions and insertions can be detected by a change in size of the amplified  
15 product in comparison to the normal genotype.

Point mutations can be identified by hybridizing amplified DNA to radiolabeled RNA of the invention or alternatively, radiolabeled antisense DNA sequences of the invention. Sequence changes at specific locations may also be revealed by nuclease protection assays, such as RNase and S1 protection or the  
20 chemical cleavage method (e.g. Cotton, *et al.* *Proc. Natl. Acad. Sci. USA*, 85:4397-4401, (1985)), or by differences in melting temperatures. "Molecular beacons" (Kostrikis L.G. *et al.*, *Science* 279:1228-1229, (1998)), hairpin-shaped, single-stranded synthetic oligo- nucleotides containing probe sequences which are complementary to the nucleic acid of the present invention, may also be used  
25 to detect point mutations or other sequence changes as well as monitor expression levels of variant product. Such diagnostics would be particularly useful for prenatal testing.

Another method for detecting mutations uses two DNA probes which are designed to hybridize to adjacent regions of a target, with abutting bases, where  
30 the region of known or suspected mutation(s) is at or near the abutting bases.

The two probes may be joined at the abutting bases, e.g., in the presence of a ligase enzyme, but only if both probes are correctly base paired in the region of probe junction. The presence or absence of mutations is then detectable by the presence or absence of ligated probe.

5 Also suitable for detecting mutations in the variant product coding sequence are oligonucleotide array methods based on sequencing by hybridization (SBH), as described, for example, in U.S. Patent No. 5,547,839. In a typical method, the DNA target analyte is hybridized with an array of oligonucleotides formed on a microchip. The sequence of the target can then be  
10 "read" from the pattern of target binding to the array.

#### **D. Gene mapping utilizing nucleic acid sequences**

The nucleic acid sequences of the present invention are also valuable for chromosome identification. The sequence is specifically targeted to and can  
15 hybridize with a particular location on an individual human chromosome. Moreover, there is a current need for identifying particular sites on the chromosome. Few chromosome marking reagents based on actual sequence data (repeat polymorphisms) are presently available for marking chromosomal location. The mapping of DNAs to chromosomes according to the present  
20 invention is an important first step in correlating those sequences with genes associated with disease.

Briefly, sequences can be mapped to chromosomes by preparing PCR primers (preferably 20-30 bp) from the variant cDNA. Computer analysis of the 3' untranslated region is used to rapidly select primers that do not span more than  
25 one exon in the genomic DNA, which would complicate the amplification process. These primers are then used for PCR screening of somatic cell hybrids containing individual human chromosomes. Only those hybrids containing the human gene corresponding to the primer will yield an amplified fragment.

PCR mapping of somatic cell hybrids or using instead radiation hybrids  
30 are rapid procedures for assigning a particular DNA to a particular chromosome.

Using the present invention with the same oligonucleotide primers, sublocalization can be achieved with panels of fragments from specific chromosomes or pools of large genomic clones in an analogous manner. Other mapping strategies that can similarly be used to map to its chromosome include *in situ* hybridization, prescreening with labeled flow-sorted chromosomes and preselection by hybridization to construct chromosome specific-cDNA libraries.

Fluorescence *in situ* hybridization (FISH) of a cDNA clone to a metaphase chromosomal spread can be used to provide a precise chromosomal location in one step. This technique can be used with cDNA as short as 50 or 60 bases. For a review of this technique, see Verma *et al.*, *Human Chromosomes: a Manual of Basic Techniques*, (1988) Pergamon Press, New York.

Once a sequence has been mapped to a precise chromosomal location, the physical position of the sequence on the chromosome can be correlated with genetic map data. Such data are found, for example, in the OMIM database (Center for Medical Genetics, Johns Hopkins University, Baltimore, MD and National Center for Biotechnology Information, National Library of Medicine, Bethesda, MD). The OMIM gene map presents the cytogenetic map location of disease genes and other expressed genes. The OMIM database provides information on diseases associated with the chromosomal location. Such associations include the results of linkage analysis mapped to this interval, and the correlation of translocations and other chromosomal aberrations in this area with the advent of polygenic diseases, such as cancer, in general and prostate cancer in particular.

### E. Therapeutic applications of nucleic acid sequences

Nucleic acid sequences of the invention may also be used for therapeutic purposes. Turning first to the second aspect of the invention (i.e. inhibition of expression of variant), expression of variant product may be modulated through antisense technology, which controls gene expression through hybridization of complementary nucleic acid sequences, i.e. antisense DNA or RNA, to the control, 5' or regulatory regions of the gene encoding variant product. For example, the 5' coding portion of the nucleic acid sequence sequence which codes for the product of the present invention is used to design an antisense oligonucleotide of from about 10 to 40 base pairs in length. Oligonucleotides derived from the transcription start site, e.g. between positions -10 and +10 from the start site, are preferred. An antisense DNA oligonucleotide is designed to be complementary to a region of the nucleic acid sequence involved in transcription (Lee *et al.*, *Nucl. Acids, Res.*, 6:3073, (1979); Cooney *et al.*, *Science* 241:456, (1988); and Dervan *et al.*, *Science* 251:1360, (1991)), thereby preventing transcription and the production of the variant products. An antisense RNA oligonucleotide hybridizes to the mRNA *in vivo* and blocks translation of the mRNA molecule into the variant products (Okano *J. Neurochem.* 56:560, (1991)). The antisense constructs can be delivered to cells by procedures known in the art such that the antisense RNA or DNA may be expressed *in vivo*. The antisense may be antisense mRNA or DNA sequence capable of coding such antisense mRNA. The antisense mRNA or the DNA coding thereof can be complementary to the full sequence of nucleic acid sequences coding for the variant protein or to a fragment of such a sequence which is sufficient to inhibit production of a protein product.

Turning now to the first aspect of the invention, i.e. expression of variant, expression of variant product may be increased by providing coding sequences for coding for said product under the control of suitable control elements ending its expression in the desired host.



The nucleic acid sequences of the invention may be employed in combination with a suitable pharmaceutical carrier. Such compositions comprise a therapeutically effective amount of the compound, and a pharmaceutically acceptable carrier or excipient. Such a carrier includes but is not limited to saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. The  
5 formulation should suit the mode of administration.

The products of the invention as well as any activators and deactivators compounds (see below) which are polypeptides, may also be employed in accordance with the present invention by expression of such polypeptides *in vivo*,  
10 which is often referred to as "*gene therapy*." Cells from a patient may be engineered with a nucleic acid sequence (DNA or RNA) encoding a polypeptide *ex vivo*, with the engineered cells then being provided to a patient to be treated with the polypeptide. Such methods are well-known in the art. For example, cells may be engineered by procedures known in the art by use of a retroviral particle  
15 containing RNA encoding a polypeptide of the present invention.

Similarly, cells may be engineered *in vivo* for expression of a polypeptide *in vivo* by procedures known in the art. As known in the art, a producer cell for producing a retroviral particle containing RNA encoding the polypeptide of the present invention may be administered to a patient for engineering cells *in vivo*  
20 and expression of the polypeptide *in vivo*. These and other methods for administering a product of the present invention by such method should be apparent to those skilled in the art from the teachings of the present invention. For example, the expression vehicle for engineering cells may be other than a retrovirus, for example, an adenovirus which may be used to engineer cells *in*  
25 *vivo* after combination with a suitable delivery vehicle.

Retroviruses from which the retroviral plasmid vectors mentioned above may be derived include, but are not limited to, Moloney Murine Leukemia Virus, spleen necrosis virus, retroviruses such as Rous Sarcoma Virus, Harvey Sarcoma Virus, avian leukosis virus, gibbon ape leukemia virus, human immunodeficiency  
30 virus, adenovirus, Myeloproliferative Sarcoma Virus, and mammary tumor virus.

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The retroviral plasmid vector is employed to transduce packaging cell lines to form producer cell lines. Examples of packaging cells which may be transfected include, but are not limited to, the *PE501*, *PA317*, *psi-2*, *psi-AM*, *PA12*, *T19-14X*, *VT-19-17-H2*, *psi-CRE*, *psi-CRIP*, *GP+E-86*, *GP+envAm12*,  
5 and *DAN* cell lines as described in Miller (*Human Gene Therapy*, Vol. 1, pg. 5-14, (1990)). The vector may transduce the packaging cells through any means known in the art. Such means include, but are not limited to, electroporation, the use of liposomes, and  $\text{CaPO}_4$  precipitation. In one alternative, the retroviral plasmid vector may be encapsulated into a liposome, or coupled to a  
10 lipid, and then administered to a host.

The producer cell line generates infectious retroviral vector particles which include the nucleic acid sequence(s) encoding the polypeptides. Such retroviral vector particles then may be employed, to transduce eukaryotic cells, either *in vitro* or *in vivo*. The transduced eukaryotic cells will express the nucleic  
15 acid sequence(s) encoding the polypeptide. Eukaryotic cells which may be transduced include, but are not limited to, embryonic stem cells, embryonic carcinoma cells, as well as hematopoietic stem cells, hepatocytes, fibroblasts, myoblasts, keratinocytes, endothelial cells, and bronchial epithelial cells.

The genes introduced into cells may be placed under the control of  
20 inducible promoters, such as the radiation-inducible *Egr-1* promoter, (Maceri, H.J., *et al.*, *Cancer Res.*, 56(19):4311 (1996)), to stimulate variant production or antisense inhibition in response to radiation, eg., radiation therapy for treating tumors.

### 25 **Example III. Variant product**

The substantially purified variant product of the invention has been defined above as the product coded from the nucleic acid sequence of the invention. Preferably the amino acid sequence is an amino acid sequence having at least 90% identity to any one of the sequences identified as SEQ ID NO: 88 to  
30 SEQ ID NO: 174 provided that the amino acid sequence is not identical to that of

the original sequence from which it has been varied. The protein or polypeptide may be in mature and/or modified form, also as defined above. Also contemplated are protein fragments having at least 10 contiguous amino acid residues, preferably at least 10-20 residues, derived from the variant product, as well as homologues as explained above.

The sequence variations are preferably those that are considered conserved substitutions, as defined above. Thus, for example, a protein with a sequence having at least 90% sequence identity with any of the products identified as SEQ ID NO: 88 to SEQ ID NO: 174, preferably by utilizing conserved substitutions as defined above is also part of the invention, and provided that it is not identical to the original peptide from which it has been varied. In a more specific embodiment, the protein has or contains any one of the sequence identified as SEQ ID NO: 88 to SEQ ID NO: 174. The variant product may be (i) one in which one or more of the amino acid residues in a sequence listed above are substituted with a conserved or non-conserved amino acid residue (preferably a conserved amino acid residue), or (ii) one in which one or more of the amino acid residues includes a substituent group, or (iii) one in which the variant product is fused with another compound, such as a compound to increase the half-life of the protein (for example, polyethylene glycol (PEG)), or a moiety which serves as targeting means to direct the protein to its target tissue or target cell population (such as an antibody), or (iv) one in which additional amino acids are fused to the variant product. Such fragments, variants and derivatives are deemed to be within the scope of those skilled in the art from the teachings herein.

#### 25 A. Preparation of variant product

Recombinant methods for producing and isolating the variant product, and fragments of the protein are described above.

In addition to recombinant production, fragments and portions of variant product may be produced by direct peptide synthesis using solid-phase techniques (cf. Stewart *et al.*, (1969) Solid-Phase Peptide Synthesis, WH Freeman Co, San

Francisco; Merrifield J., *J. Am. Chem. Soc.*, **85**:2149-2154, (1963)). In vitro peptide synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer, Foster City, Calif.) in accordance with  
5 the instructions provided by the manufacturer. Fragments of variant product may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

#### **B. Therapeutic uses and compositions utilizing the variant product**

10

The variant product of the invention is generally useful in treating diseases and disorders which are characterized by a lower than normal level of variant expression, and or diseases which can be cured or ameliorated by raising the level of the variant product, even if the level is normal.

15

Variant products or fragments may be administered by any of a number of routes and methods designed to provide a consistent and predictable concentration of compound at the target organ or tissue. The product-containing compositions may be administered alone or in combination with other agents, such as stabilizing compounds, and/or in combination with other pharmaceutical  
20 agents such as drugs or hormones.

20

Variant product-containing compositions may be administered by a number of routes including, but not limited to oral, intravenous, intramuscular, transdermal, subcutaneous, topical, sublingual, or rectal means as well as by nasal application. Variant product-containing compositions may also be administered  
25 via liposomes. Such administration routes and appropriate formulations are generally known to those of skill in the art.

25

The product can be given via intravenous or intraperitoneal injection. Similarly, the product may be injected to other localized regions of the body. The product may also be administered via nasal insufflation. Enteral administration is  
30 also possible. For such administration, the product should be formulated into an

30

appropriate capsule or elixir for oral administration, or into a suppository for rectal administration.

The foregoing exemplary administration modes will likely require that the product be formulated into an appropriate carrier, including ointments, gels, 5 suppositories. Appropriate formulations are well known to persons skilled in the art.

Dosage of the product will vary, depending upon the potency and therapeutic index of the particular polypeptide selected.

A therapeutic composition for use in the treatment method can include the 10 product in a sterile injectable solution, the polypeptide in an oral delivery vehicle, the product in an aerosol suitable for nasal administration, or the product in a nebulized form, all prepared according to well known methods. Such compositions comprise a therapeutically effective amount of the compound, and a pharmaceutically acceptable carrier or excipient. Such a carrier includes but is not 15 limited to saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. The product of the invention may also be used to modulate endothelial differentiation and proliferation as well as to modulate apoptosis either *ex vivo* or *in vitro*, for example, in cell cultures.

#### 20 **Example IV. Screening methods for activators and deactivators (inhibitors)**

The present invention also includes an assay for identifying molecules, such as synthetic drugs, antibodies, peptides, or other molecules, which have a modulating effect on the activity of the variant product, e.g. activators or 25 deactivators of the variant product of the present invention. Such an assay comprises the steps of providing an variant product encoded by the nucleic acid sequences of the present invention, contacting the variant protein with one or more candidate molecules to determine the candidate molecules modulating effect on the activity of the variant product, and selecting from the molecules a 30 candidate's molecule capable of modulating variant product physiological activity.

The variant product, its catalytic or immunogenic fragments or oligopeptides thereof, can be used for screening therapeutic compounds in any of a variety of drug screening techniques. The fragment employed in such a test may be free in solution, affixed to a solid support, borne on a cell membrane or located intracellularly. The formation of binding complexes, between variant product and the agent being tested, may be measured. Alternatively, the activator or deactivator may work by serving as agonist or antagonist, respectively, of the variant receptor, binding entity or target site, and their effect may be determined in connection with any of the above.

Another technique for drug screening which may be used provides for high throughput screening of compounds having suitable binding affinity to the variant product is described in detail by Geysen in PCT Application WO 84/03564, published on Sep. 13, 1984. In summary, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. The peptide test compounds are reacted with the full variant product or with fragments of variant product and washed. Bound variant product is then detected by methods well known in the art. Substantially purified variant product can also be coated directly onto plates for use in the aforementioned drug screening techniques. Alternatively, non-neutralizing antibodies can be used to capture the peptide and immobilize it on a solid support.

Antibodies to the variant product, as described in Example VI below, may also be used in screening assays according to methods well known in the art. For example, a "sandwich" assay may be performed, in which an anti-variant antibody is affixed to a solid surface such as a microtiter plate and variant product is added. Such an assay can be used to capture compounds which bind to the variant product. Alternatively, such an assay may be used to measure the ability of compounds to influence with the binding of variant product to the variant receptor, and then select those compounds which effect the binding.

## Example V. Anti-variant antibodies

### A. Synthesis

In still another aspect of the invention, the purified variant product is used to produce anti-variant antibodies which have diagnostic and therapeutic uses related to the activity, distribution, and expression of the variant product.

Antibodies to the variant product may be generated by methods well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, humanized, single chain, Fab fragments and fragments produced by an Fab expression library. Antibodies, i.e., those which inhibit dimer formation, are especially preferred for therapeutic use.

A fragment of the variant product for antibody induction does not require biological activity but have to feature immunological activity; however, the protein fragment or oligopeptide must be antigenic. Peptides used to induce specific antibodies may have an amino acid sequence consisting of at least five amino acids, preferably at least 10 amino acids of the sequences specified in any one of SEQ ID NO: 88 to SEQ ID NO: 174. Preferably they should mimic a portion of the amino acid sequence of the natural protein and may contain the entire amino acid sequence of a small, naturally occurring molecule. Short stretches of variant protein amino acids may be fused with those of another protein such as keyhole limpet hemocyanin and antibody produced against the chimeric molecule. Procedures well known in the art can be used for the production of antibodies to variant product.

For the production of antibodies, various hosts including goats, rabbits, rats, mice, etc may be immunized by injection with variant product or any portion, fragment or oligopeptide which retains immunogenic properties. Depending on the host species, various adjuvants may be used to increase immunological response. Such adjuvants include but are not limited to Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet

hemocyanin, and dinitrophenol. BCG (bacilli Calmette-Guerin) and *Corynebacterium parvum* are potentially useful human adjuvants.

Monoclonal antibodies to variant protein may be prepared using any technique which provides for the production of antibody molecules by continuous  
5 cell lines in culture. These include but are not limited to the hybridoma technique originally described by Koehler and Milstein (*Nature* 256:495-497, (1975)), the human B-cell hybridoma technique (Kosbor *et al.*, *Immunol. Today* 4:72, (1983); Cote *et al.*, *Proc. Natl. Acad. Sci.* 80:2026-2030, (1983)) and the EBV-hybridoma technique (Cole, *et al.*, *Mol. Cell Biol.* 62:109-120, (1984)).

10 Techniques developed for the production of "chimeric antibodies", the splicing of mouse antibody genes to human antibody genes to obtain a molecule with appropriate antigen specificity and biological activity can also be used (Morrison *et al.*, *Proc. Natl. Acad. Sci.* 81:6851-6855, (1984); Neuberger *et al.*, *Nature* 312:604-608, (1984); Takeda *et al.*, *Nature* 314:452-454, (1985)).  
15 Alternatively, techniques described for the production of single chain antibodies (U.S. Pat. No. 4,946,778) can be adapted to produce single-chain antibodies specific for the variant protein.

Antibodies may also be produced by inducing *in vivo* production in the lymphocyte population or by screening recombinant immunoglobulin libraries or  
20 panels of highly specific binding reagents as disclosed in Orlandi *et al.* (*Proc. Natl. Acad. Sci.* 86:3833-3837, 1989)), and Winter G and Milstein C., (*Nature* 349:293-299, (1991)).

Antibody fragments which contain specific binding sites for variant protein may also be generated. For example, such fragments include, but are not  
25 limited to, the F(ab')<sub>2</sub> fragments which can be produced by pepsin digestion of the antibody molecule and the Fab fragments which can be generated by reducing the disulfide bridges of the F(ab')<sub>2</sub> fragments. Alternatively, Fab expression libraries may be constructed to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity (Huse W.D. *et al.*, *Science*  
30 256:1275-1281, (1989)).



## B. Diagnostic applications of antibodies

A variety of protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the  
5 formation of complexes between the variant product and its specific antibody and the measurement of complex formation. A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two noninterfering epitopes on a specific variant product is preferred, but a competitive binding assay may also be employed. These assays are described in Maddox D.E., *et al.*,  
10 (*J. Exp. Med.* 158:1211, (1983)).

Antibodies which specifically bind variant product are useful for the diagnosis of conditions or diseases characterized by expression of the novel variant of the invention (where normally it is not expressed) by over or under expression of variant as well as for detection of diseases in which the proportion  
15 between the amount of the variants of the invention and the original sequence from which it varied is altered. Alternatively, such antibodies may be used in assays to monitor patients being treated with variant product, its activators, or its deactivators. Diagnostic assays for variant protein include methods utilizing the antibody and a label to detect variant product in human body fluids or extracts of  
20 cells or tissues. The products and antibodies of the present invention may be used with or without modification. Frequently, the proteins and antibodies will be labeled by joining them, either covalently or noncovalently, with a reporter molecule. A wide variety of reporter molecules are known in the art.

A variety of protocols for measuring the variant product, using either  
25 polyclonal or monoclonal antibodies specific for the respective protein are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescent activated cell sorting (FACS). As noted above, a two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on variant product is  
30 preferred, but a competitive binding assay may be employed. These assays are

described, among other places, in Maddox, *et al. (supra)*. Such protocols provide a basis for diagnosing altered or abnormal levels of variant product expression. Normal or standard values for variant product expression are established by combining body fluids or cell extracts taken from normal subjects, preferably human, with antibody to variant product under conditions suitable for complex formation which are well known in the art. The amount of standard complex formation may be quantified by various methods, preferably by photometric methods. Then, standard values obtained from normal samples may be compared with values obtained from samples from subjects potentially affected by disease. Deviation between standard and subject values establishes the presence of disease state.

The antibody assays are useful to determine the level of variant product present in a body fluid sample, in order to determine whether it is being expressed at all, whether it is being overexpressed or underexpressed in the tissue, or as an indication of how variant levels of variable products are responding to drug treatment.

By another aspect the invention concerns methods for determining the presence or level of various anti-variant antibodies in a biological sample obtained from patients, such as blood or serum sample using as an antigen the variant product. Determination of said antibodies may be indicative to a plurality of pathological conditions or diseases.

### **C. Therapeutic uses of antibodies**

In addition to their diagnostic use the antibodies may have a therapeutical utility in blocking or decreasing the activity of the variant product in pathological conditions where beneficial effect can be achieved by such a decrease.

The antibody employed is preferably a humanized monoclonal antibody, or a human Mab produced by known globulin-gene library methods. The antibody is administered typically as a sterile solution by IV injection, although other parenteral routes may be suitable. Typically, the antibody is administered

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in an amount between about 1-15 mg/kg body weight of the subject. Treatment is continued, e.g., with dosing every 1-7 days, until a therapeutic improvement is seen.

Although the invention has been described with reference to specific  
5 methods and embodiments, it is appreciated that various modifications and changes may be made without departing from the invention.

### **Example VI. Expression of ACEV**

#### **(a) Immunohistochemical staining:**

The immunohistochemical staining was performed using Histostain plus Kit  
10 (Zymed Laboratories Inc.). Mouse salivary gland micron sections were prepared using a R. Gung microtome and fixed on superfrost plus slides with 2% Tespa. Deparaffinization was performed in xylene for 10 min. Dehydration was performed three times in absolute ethanol and once 95% ethanol. The slides were washed in DDW and then incubated with 3% H<sub>2</sub>O for 5 min. Subsequently, the slide were washed in  
15 DDW and twice in 0.05M TrisHCl pH 7.6 (Optimax wash Buffer, BioGenex). The rest of the procedure was performed following the manufacturer's instructions. The results are shown in Figs. 88 and 89.

The immunohistochemical staining was performed on mouse salivary gland  
20 micron sections. The immunohistochemistry was done using specific polyclonal antibodies designed against the c-terminus of SEQ ID NO: 144 (12 amino-acids), which are unique to said ACEV product and lack in the original ACE protein (Fig 88-a,b,d magnification X 100; Fig 89-b magnification X 400) compared with the pre-immune rabbit's serum (Fig 88-c, Fig. 89-a).

25 ACE was found to express in ductal epifilus (Fig 88-a,b,d, Fig 89-b).

The same procedure was repeated for mouse lymph node sectors stained with pre-immune serum (Fig. 90a, 90c - magnifications X 100, X 200, respectively) and immune serum (Fig. 90b and 90c magnifications X 100, X 200 respectively).

The results show positive staining in salivary glands.

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(b) RT - PCR

RNA Purification and cDNA Synthesis Total RNA was extracted from different mouse tissues using Tri-Reagent System (Molecular Research Center, Inc., Cincinnati, OH). Synthesis of first-strand cDNA was carried out using Oligo(dT)15 (Promega, 5 Madison, WI), Superscript II (Gibco/BRL, Gaithersburg, MD), Rnasin (Promega, Madison, WI) and dNTP's (Gibco/BRL, Gaithersburg, MD). + with Superscript II, - without Superscript II.

Polymerase Chain Reaction (PCR): PCR was performed using Expand Long Template PCR system (Roche). As a template cDNA from different tissues was used. 10 The PCR reaction on PTC-225 (MJ Research, Inc.). PCR products were analyzed on an automated DNA sequencer ABI Prizem 310 Genetic Analyzer (Perkin Elmer).

The results are shown in Fig. 91. As can be seen the ACEV of the invention was expressed in skin, lung, heart, thymus, spleen, bone marrow and brain tissue

**CLAIMS:**

1. An isolated nucleic acid sequence, of an alternative splicing variant, selected from the group consisting of:
  - (i) the nucleic acid sequence depicted in any one of SEQ ID NO: 1 to  
5 SEQ ID NO: 87;
  - (ii) nucleic acid sequences having at least 90% identity with the sequence of (i) with the proviso that each sequence is different than the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing; and
  - 10 (iii) fragments of (i) or (ii) of at least 20 b.p., provided that said fragment contains a sequence which is not present, as a continuous stretch of nucleotides, in the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing.
2. An isolated nucleic acid sequence complementary to the nucleic acid  
15 sequence of Claim 1.
3. An amino acid sequence selected from the group consisting of:
  - (i) an amino acid sequence coded by the isolated nucleic acid sequence of alternative splice variants of Claim 1;
  - (ii) homologues of the amino acid sequences of (i) in which one or more  
20 amino acids has been added, deleted, replaced or chemically modified in the region or adjacent to the region where the amino acid sequences differs from the original amino acid sequence, coded by the original nucleic acid sequence from which the variant has been varied.
- 25 4. An amino acid sequence according to Claim 3, as depicted in any one of SEQ ID NO: 88 to SEQ ID NO: 174.
5. An isolated nucleic acid sequence coding for any one of the amino acid sequences of Claim 3 or 4.
6. A purified antibody which binds specifically to any of the amino acid  
30 sequence of Claim 3 or 4.

7. An expression vector comprising any one of the nucleic acid sequences of Claim 1 or 5 and control elements for the expression of the nucleic acid sequence in a suitable host.
8. An expression vector comprising any one of the nucleic acid sequences of Claim 2, and control elements for the expression of the nucleic acid sequences in a suitable host.
9. A host cell transfected by the expression vector of Claim 7 or 8.
10. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:
  - (i) the expression vector of Claim 7; and
  - (ii) any one of the amino acid sequences of Claim 3 or 4.
11. A pharmaceutical composition according to Claim 10, for treatment of diseases which can be ameliorated or cured by raising the level of any one of the amino acid sequences depicted in SEQ ID NO: 88 to SEQ ID NO: 174.
12. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:
  - (i) any one of the nucleic acid sequences of Claim 2;
  - (ii) the expression vector of Claim 8; and
  - (iii) the purified antibody of Claim 6.
13. A pharmaceutical composition according to Claim 12, for treatment of diseases which can be ameliorated or cured by decreasing the level of any one of the amino acid sequences depicted in SEQ ID NO: 88 to SEQ ID NO: 174.
14. A method for detecting an variant nucleic acid sequence in a biological sample, comprising the steps of:
  - (a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1 or 2; and
  - (b) detecting said hybridization complex;wherein the presence of said hybridization complex correlates with the presence of an variant nucleic acid sequence in the said biological sample.
15. A method for determining the level of variant nucleic acid sequences in a biological sample comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 1 or 2; and

(b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

16. A method for determining the ratio between the level of variant of the nucleic acid sequence in a first biological sample and the level of the original sequence from which the variant has been varied by alternative splicing in a second biological sample comprising:

10 (a) determining the level of the variant nucleic acid sequence in the first biological sample according to the method of Claim 15;

(b) determining the level of the original sequence in the second biological sample; and

(c) comprising the levels obtained in (a) and (b) to give said ratio.

15 17. A method according to Claim 16, wherein said first and said second biological samples are the same sample.

18. A method according to any of Claims 14 to 17, wherein the nucleic acid material of said biological sample are mRNA transcripts.

19. A method according to Claim 18, where the nucleic acid sequence is present in a nucleic acid chip.

20. A method for identifying candidate compounds capable of binding to the variant product and modulating its activity the method comprising:

(i) providing any one of the amino acid sequences as defined in Claim 3 or 4;

25 (ii) contacting a candidate compound with said amino acid sequence;

(iii) determining the effect of said candidate compound on the biological activity of said protein or polypeptide and selecting those compounds which show a significant effect on said biological activity.

21. A method according to Claim 20, wherein the compound is an activator and the measured effect is increase in the biological activity.

22. A method according to Claim 20, wherein the compound is an deactivator and the effect is decrease in the biological activity.
23. An activator of any one of the amino acid sequences of Claim 3 or 4.
24. An deactivator of any one of the amino acid sequences of Claims 3 or 4.
- 5 25. A method for detecting any one of the amino acid sequences of Claim 3 or 4 in a biological sample, comprising the steps of:
- (a) contacting with said biological sample the antibody of Claim 8, thereby forming an antibody-antigen complex; and
  - (b) detecting said antibody-antigen complex
- 10 wherein the presence of said antibody-antigen complex correlates with the presence of the desired amino acid in said biological sample.
26. A method for detecting the level of the amino acid sequence of any one of Claim 3 or 4 in a biological sample, comprising the steps of:
- (a) contacting with said biological sample the antibody of Claim 8,
- 15 thereby forming an antibody-antigen complex; and
- (b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the level of said amino acid sequence in the sample.
27. A method for determining the ratio between the level of any one of the
- 20 amino acid sequences of Claims 3 or 4 present in a first biological sample and the level of the original amino acid sequences from which they were varied by alternative splicing, present in a second biological sample, the method comprising:
- (a) determining the level of the amino acid sequences of Claims 3 or 4 into a first sample by the method of Claim 26;
- 25 (b) determining the level of the original amino acid sequence in the second sample; and
- (c) comparing the level obtained in (a) and (b) to give said ratio.
28. A method according to Claim 27, wherein said first and said second biological samples are the same sample.
- 30 29. A method for detecting any one of the antibodies of Claim 6 in a biological sample comprising the steps of:



(a) contacting said biological sample with any one of the amino acid sequences of Claim 3 or 4 thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

wherein the presence of said antibody-antigen complex correlates with the presence of the antibody in said biological sample.

30. A method for detecting the level of any one of the antibodies of Claim 6 in a biological sample comprising the steps of:

(a) contacting said biological sample with any one of the amino acid sequences of Claim 3;

(b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the levels of said antibody in the sample.

31. An isolated nucleic acid sequence according to Claim 1 of an alternative splicing variant of an angiotensin converting enzyme (ACEV) selected from the group consisting of:

(i) the nucleic acid sequence depicted in SEQ ID NO: 57 or SEQ ID NO: 85;

(ii) nucleic acid sequences having at least 90% identity with the sequence of (i) with the proviso that each sequence is different than the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing; and

(iii) fragments of (i) or (ii) of at least 20 b.p., provided that said fragment contains a sequence which is not present, as a continuous stretch of nucleotides, in the original nucleic acid sequence from which the sequences of (i) have been varied by alternative splicing.

32. An isolated nucleic acid sequence complementary to the nucleic acid sequence of Claim 31.

33. An amino acid sequence selected from the group consisting of:

(i) an amino acid sequence coded by the isolated nucleic acid sequence of alternative splice variants of Claim 31;

(ii) homologues of the amino acid sequences of (i) in which one or more amino acids has been added, deleted, replaced or chemically modified in the region

or adjacent to the region where the amino acid sequences differs from the original amino acid sequence, coded by the original nucleic acid sequence from which the variant has been varied.

34. An amino acid sequence according to Claim 33, as depicted in SEQ ID NO:  
5 144 or SEQ ID NO: 172.
35. An isolated nucleic acid sequence coding for any one of the amino acid sequences of Claim 33 or 34.
36. A purified antibody which binds specifically to any of the amino acid sequence of Claim 33 or 34.
- 10 37. An expression vector comprising any one of the nucleic acid sequences of Claim 31 or 35 and control elements for the expression of the nucleic acid sequence in a suitable host.
38. An expression vector comprising any one of the nucleic acid sequences of Claim 32, and control elements for the expression of the nucleic acid sequences in a  
15 suitable host.
39. A host cell transfected by the expression vector of Claim 37 or 38.
40. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and as an active ingredient an agent selected from the group consisting of:
- (i) the expression vector of Claim 37; and
  - 20 (ii) any one of the amino acid sequences of Claim 33 or 34.
41. A pharmaceutical composition according to Claim 40, for treatment of diseases which can be ameliorated or cured by raising the level of any one of the amino acid sequences depicted in SEQ ID NO: 144 or SEQ ID NO: 172.
42. A pharmaceutical composition comprising a pharmaceutically acceptable  
25 carrier and as an active ingredient an agent selected from the group consisting of:
- (i) any one of the nucleic acid sequences of Claim 32;
  - (ii) the expression vector of Claim 38; and
  - (iii) the purified antibody of Claim 36.
43. A pharmaceutical composition according to Claim 42, for treatment of  
30 diseases which can be ameliorated or cured by decreasing the level of the amino acid sequences depicted in SEQ ID NO: 144 or SEQ ID NO: 172.

44. A pharmaceutical composition according to Claim 40 or 42 for the treatment of a disease selected from: cardiovascular disorders, congestive heart failure, hypertension, renal hypertension, diabetes, multiple sclerosis, sarcoidosis, nonsarcoidotic pulmonary granulomatous diseases, vascular pathologies involving  
5 an endothelial abnormality and cancer.

45. A method for detecting an variant nucleic acid sequence in a biological sample, comprising the steps of:

(a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 31 or 32; and

10 (b) detecting said hybridization complex;

wherein the presence of said hybridization complex correlates with the presence of an variant nucleic acid sequence in the said biological sample.

46. A method for determining the level of variant nucleic acid sequences in a biological sample comprising the steps of:

15 (a) hybridizing to nucleic acid material of said biological sample any one of the nucleic acid sequences of Claim 31 or 32; and

(b) determining the amount of hybridization complexes and normalizing said amount to provide the level of the variant nucleic acid sequences in the sample.

20 47. A method for determining the ratio between the level of variant of the nucleic acid sequence in a first biological sample and the level of the original sequence from which the variant has been varied by alternative splicing in a second biological sample comprising:

(a) determining the level of the variant nucleic acid sequence in the first  
25 biological sample according to the method of Claim 46;

(b) determining the level of the original sequence in the second biological sample; and

(c) comprising the levels obtained in (a) and (b) to give said ratio.

48. A method according to Claim 47, wherein said first and said second  
30 biological samples are the same sample.

49. A method according to any of Claims 45 to 48, wherein the nucleic acid material of said biological sample are mRNA transcripts.
50. A method according to Claim 49, where the nucleic acid sequence is present in a nucleic acid chip.
- 5 51. A method for identifying candidate compounds capable of binding to the variant product and modulating its activity the method comprising:
- (i) providing any one of the amino acid sequences as defined in Claim 33 or 34;
  - (ii) contacting a candidate compound with said amino acid sequence;
  - 10 (iii) determining the effect of said candidate compound on the biological activity of said protein or polypeptide and selecting those compounds which show a significant effect on said biological activity.
52. A method according to Claim 51, wherein the compound is an activator and the measured effect is increase in the biological activity.
- 15 53. A method according to Claim 51, wherein the compound is an deactivator and the effect is decrease in the biological activity.
54. An activator of any one of the amino acid sequences of Claim 33 or 34.
55. An deactivator of any one of the amino acid sequences of Claims 33 or 34.
56. A method for detecting any one of the amino acid sequences of Claim 33 or 20 34 in a biological sample, comprising the steps of:
- (a) contacting with said biological sample the antibody of Claim 38, thereby forming an antibody-antigen complex; and
  - (b) detecting said antibody-antigen complex
- wherein the presence of said antibody-antigen complex correlates with the 25 presence of the desired amino acid in said biological sample.
57. A method for detecting the level of the amino acid sequence of any one of Claim 33 or 34 in a biological sample, comprising the steps of:
- (a) contacting with said biological sample the antibody of Claim 38, thereby forming an antibody-antigen complex; and

(b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the level of said amino acid sequence in the sample.

58. A method for determining the ratio between the level of any one of the amino acid sequences of Claims 33 or 34 present in a first biological sample and the level of the original amino acid sequences from which they were varied by alternative splicing, present in a second biological sample, the method comprising:

(a) determining the level of the amino acid sequences of Claims 33 or 34 into a first sample by the method of Claim 57;

10 (b) determining the level of the original amino acid sequence in the second sample; and

(c) comparing the level obtained in (a) and (b) to give said ratio.

59. A method according to Claim 58, wherein said first and said second biological samples are the same sample.

15 60. A method for detecting any one of the antibodies of Claim 36 in a biological sample comprising the steps of:

(a) contacting said biological sample with any one of the amino acid sequences of Claim 3 or 4 thereby forming an antibody-antigen complex; and

(b) detecting said antibody-antigen complex

20 wherein the presence of said antibody-antigen complex correlates with the presence of the antibody in said biological sample.

61. A method for detecting the level of any one of the antibodies of Claim 36 in a biological sample comprising the steps of:

(a) contacting said biological sample with any one of the amino acid sequences of Claim 33;

25 (b) detecting the amount of said antibody-antigen complex and normalizing said amount to provide the levels of said antibody in the sample.

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1  MPIMGSSVYITVELAIAVLAILGNVLVCWAVWLNLSNLQNVTNYFVVS LAA  50
   |||||||
1  MPIMGSSVYITVELAIAVLAILGNVLVCWAVWLNLSNLQNVTNYFVVS LAA  50

51 ADIAVGVLAI PFAITISTGFCAACHGCLFIACFVLVLTQSSIFSLLAIAI  100
   |||||||
51 ADIAVGVLAI PFAITISTGFCAACHGCLFIACFVLVLTQSSIFSLLAIAI  100

101 DRYIAIRIPLRYNGLVTGTRAKGIIAICWVLSFAIGLTPMLGWNNCGQPK  150
   |||||||
101 DRYIAIRIPLRYNGLVTGTRAKGIIAICWVLSFAIGLTPMLGWNNCGQPK  150

151 EGKNHSQCGGEGQVACLFEDVVPNMNMYVFNFFACVLVPLLMLGVYLRI  200
   |||||||
151 EGKNHSQCGGEGQVACLFEDVVPNMNMYVFNFFACVLVPLLMLGVYLRI  200

201 FLAARRQLKQMESQPLPGERARSTLQKEVHAAKSLA.....PLH  239
   |||||||
201 FLAARRQLKQMESQPLPGERARSTLQKEVHAAKSLAIVGLFALCWLPLH  250

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FIG. 1



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1 MPRYGASLRQSCPRSGREQGDGTAGAPGLLWMLVLALALALALSDS 90
  |||||
1 MPRYGASLRQSCPRSGREQGDGTAGAPGLLWMLVLALALALALSDS 48

.
91 RVLWAPAEAHPLSPQGHPARLHRIVPRLRDVFGWGNLTCPICKGLFTAIN 140
  |||||
49 RVLWAPAEAHPLSPQGHPARLHRIVPRLRDVFGWGNLTCPICKGLFTAIN 98

.
141 LGLKKEPNVARVGSVAIKLCNLLKIAPPAVCQSIVHLFEDDMVEVWRRSV 190
  |||||
99 LGLKKEPNVARVGSVAIKLCNLLKIAPPAVCQSIVHLFEDDMVEVWRRSV 148

.
191 LSPSEACGLLLGSTCGHWDIFSSWNISLPTVPKPPKPPSPAPGAPVSR 240
  |||||
149 LSPSEARGLLLGSTCGHWDIFSSWNISLPTVPKPPKPPSPAPGAPVSR 198

.
241 ILFLTDLHWDHDYLEGTDPCADPLCCRRGSLPPASRPGAGYWGEYSKC 290
  |||||
199 ILFLTDLHWDHDYLEGTDPCADPLCCRRGSLPPASRPGAGYWGEYSKC 248

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**FIG. 2**



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291 DLPLRTLESLLSGLGPAGPFDMVYWTGDIPAHDVWHQTRQDQLRALTTVT 340
    |||||
249 DLPLRTLESLLSGLGPAGPFDMVYWTGDIPAHDVWHQTRQDQLRALTTVT 298

341 ALVRKFLGPVPVYPVAVGNHESHPVNSFPFPIEGNHSSRWLYEAMAKAWE 390
    |||||
299 ALVRKFLGPVPVYPVAVGNHESHPVNSFPFPIEGNHSSRWLYEAMAKAWE 348

391 PWLPAAEALRTLRIIGGFYALSPYPGLRLISLNMNFCSENFWLLINSTDPA 440
    |||||
349 PWLPAAEALRTLRIIGGFYALSPYPGLRLISLNMNFCSENFWLLINSTDPA 398

441 GQLQWLVGELQAAEDRGDKVHIIGHIPPGHCLKSWSWNNYYRIVARYENTL 490
    |||||
399 GQLQWLVGELQAAEDRGDKVHIIGHIPPGHCLKSWSWNNYYRIVARYENTL 448

491 AAQFFGHTHVDEFEFYDEETLSRPLAVAF LAPSATYI GLNPLVSEAE G 540
    |||||
449 AAQFFGHTHVDEFEFYDEETLSRPLAVAF LAPSATYI GLNP ..... 491

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FIG. 2 (CONT.<sup>1</sup>)

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541 SLPYPGVGGIGEGGWSQSLQSMGRMCGPSLELPLLAPPVSPVTSLAGYRV 590
      ||||
492 .....GYRV 495

591 YQIDGNYSGSSHVVLDHETIILNLTQANIPGAIPHWQLLYRARETYGLPN 640
      |||||
496 YQIDGNYSGSSHVVLDHETIILNLTQANIPGAIPHWQLLYRARETYGLPN 545

641 TLP TAWHNLVYRMRGDMQLFQTFWFLYHKGHPPEPCGTPCRLATLCAQL 690
      |||||
546 TLP TAWHNLVYRMRGDMQLFQTFWFLYHKGHPPEPCGTPCRLATLCAQL 595

      691 SARADSPALCRHLMPPDGS LPEAQSLWPRPLFC 722
      |||||
      596 SARADSPALCRHLMPPDGS LPEAQSLWPRPLFC 627

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FIG. 2 (CONT.<sup>2</sup>)

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1  LLLGFLVLESTLSIPPWEAPKEHKYKAEHTVVLTVTGEPCHEPFQY  50
   | | | | | | | | | | | | | | | | | | | | | | | | | | | |
4  LLLGFLVLESTLSIPPWEAPKEHKYKAEHTVVLTVTGEPCHEPFQY  53
   .
51 HRQLYHKCTHKGRPGPQPCWCATTPNFDQDQRWGYCLEPKKVVDHCSKHSP  100
   | | | | | | | | | | | | | | | | | | | | | | | | | | | |
54 HRQLYHKCTHKGRPGPQPCWCATTPNFDQDQRWGYCLEPKKVVDHCSKHSP  103
   .
101 CQKGGTCVNMPSPGPHCLCPQHLLTGNHCQKEKCFEPQLLRFHKNKIWYRT  150
   | | | | | | | | | | | | | | | | | | | | | | | | | | | |
104 CQKGGTCVNMPSPGPHCLCPQHLLTGNHCQKEKCFEPQLLRFHKNKIWYRT  153
   .
151 EQAAVARCQCKGPDHAHCQRLASQACRTNPLHGGRCLEVEGHRLLCHCPVG  200
   | | | | | | | | | | | | | | | | | | | | | | | | | | | |
154 EQAAVARCQCKGPDHAHCQRLASQACRTNPLHGGRCLEVEGHRLLCHCPVG  203
   .
201 YTGPFCDVDTKASCYDGRGLSYRGLARTTSLGAPCQCPWASEATYRNVTAE  250
   | | | | | | | | | | | | | | | | | | | | | | | | | | | |
204 YTGPFCDVDTKASCYDGRGLSYRGLARTTSLGAPCQCPWASEATYRNVTAE  253
   .

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FIG. 3

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251 QARNWGLGGHAFCRNPNDIRPWCFLNRDRLSWEYCDLAQCQTPTQAAP 300
   |||||
254 QARNWGLGGHAFCRNPNDIRPWCFLNRDRLSWEYCDLAQCQTPTQAAP 303
   |||||

301 PTPVSPRLHVPLMPAQAPPKPQTTRTPPQSQTPGALPAKREQPPSLTR 350
   |||||
304 PTPVSPRLHVPLMPAQAPPKPQTTRTPPQSQTPGALPAKREQPPSLTR 353
   |||||

351 NGPLSCGQRLRKSLSSMTRVVGGGLVALRGAHPYIAALYWGHSHFCAGSLIA 400
   |||||
354 NGPLSCGQRLRKSLSSMTRVVGGGLVALRGAHPYIAALYWGHSHFCAGSLIA 403
   |||||

401 PCWVLTAAHCLQDRPAPEDLTVVLGQERRNHSCEPCQTLAVRSYRLHEAF 450
   |||||
404 PCWVLTAAHCLQDRPAPEDLTVVLGQERRNHSCEPCQTLAVRSYRLHEAF 453
   |||||

451 SPVSYQHDLALLRLQEDADGSCALLSPYVQPVCLPSGAARPSETTLCQVA 500
   |||||
454 SPVSYQHDLALLRLQEDADGSCALLSPYVQPVCLPSGAARPSETTLCQVA 503
   |||||

501 GWGHQFEAS 509
   |||||
504 GWGHQFEGA 512

```

FIG. 3 (CONT.<sup>1</sup>)

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```

1  MARLGNCSLTWAALIILLPGSLEECGHISVSAPIVHLGDPITASCIKQ  50
  |||||||||||||||||||||||||||||||||||||||||||||||
1  MARLGNCSLTWAALIILLPGSLEECGHISVSAPIVHLGDPITASCIKQ  50

51  NCSHLDPEPQILWRLGAELQPGGRQQRSLSDGTQESIITLPHLNHTQAFLS  100
  |||||||||||||||||||||||||||||||||||||||||||||||
51  NCSHLDPEPQILWRLGAELQPGGRQQRSLSDGTQESIITLPHLNHTQAFLS  100

101 CCLNWGNSLQILDQVELRAGYPPIPHNLSCLMNLTSSLICQWEPGPET  150
  |||||||||||||||||||||||||||||||||||||||||||||||
101 CCLNWGNSLQILDQVELRAGYPPIPHNLSCLMNLTSSLICQWEPGPET  150

151 HLPTSFTLKSFKSRGNCQTQGDSILDCVPKDGQSHCCIPRKHLLLYQNMG  200
  |||||||||||||||||||||||||||||||||||||||||||||||
151 HLPTSFTLKSFKSRGNCQTQGDSILDCVPKDGQSHCCIPRKHLLLYQNMG  200

201 IWVQAEALGTSMSPQLCLDPMDVVVKLEPPMLRTMDPSPEAAPQAGCLQ  250
  |||||||||||||||||||||||||||||||||||||||||||||||
201 IWVQAEALGTSMSPQLCLDPMDVVVKLEPPMLRTMDPSPEAAPQAGCLQ  250

```

FIG. 4

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```

251 LCWEPWQPGHLHINQKCELRHKPQGEASWALVGPLPLEALQYELCGLLPA 300
|||||
251 LCWEPWQPGHLHINQKCELRHKPQGEASWALVGPLPLEALQYELCGLLPA 300

301 TAYTLQIRCIRWPLPGHWS..... 320
|||||
301 TAYTLQIRCIRWPLPGHWSDSPSLELRTTERTAPTVRLDTWWRQQLDPR 350

321 .....GAILPLCNTTELSCTFHLP 339
|||||
351 TVQLFWKVPLEEDSGRIQGYVVSWRPSGQAGAILPLCNTTELSCTFHLP 400

340 SEAQEVAlVAYNSAGTSRPTPVVFESESRGPALTRLHAMARDPHSLWVGWE 389
|||||
401 SEAQEVAlVAYNSAGTSRPTPVVFESESRGPALTRLHAMARDPHSLWVGWE 450

390 PPNPWPQGYVIEWGLGPPSASNSNKTWRMEQNGRATGFLLENIRPFQLY 439
|||||
451 PPNPWPQGYVIEWGLGPPSASNSNKTWRMEQNGRATGFLLENIRPFQLY 500

```

FIG. 4 (CONT.<sup>1</sup>)

SIIRSTITITE SHEET (RII E 26)

440	EIIVTPLYQDTMGPSQHVYAYSQEMAPSHAPELHLKHIGKTWAQLEWVPE	489
501	EIIVTPLYQDTMGPSQHVYAYSQEMAPSHAPELHLKHIGKTWAQLEWVPE	550
490	PPELGKSP LTHYTI FWTNAQNQSFSA I L NASSRGFVLHGLEPASLYHIHL	539
551	PPELGKSP LTHYTI FWTNAQNQSFSA I L NASSRGFVLHGLEPASLYHIHL	600
540	MAASQAGATNSTVLTMTLTPEGSELHI I LGLFGLLLLTCLCGTAWLCC	589
601	MAASQAGATNSTVLTMTLTPEGSELHI I LGLFGLLLLTCLCGTAWLCC	650
590	SPNRKNPLWPSVDP PAHSSLGSWVPTIMEEDAFQLPGLGTPPITKLTVLE	639
651	SPNRKNPLWPSVDP PAHSSLGSWVPTIMEEDAFQLPGLGTPPITKLTVLE	700
640	EDEKKPV PWESHNSSETCGLPTLVQTYVLQGDPRAVSTQ PQSQSGTSDQV	689
701	EDEKKPV PWESHNSSETCGLPTLVQTYVLQGDPRAVSTQ PQSQSGTSDQV	750

**FIG. 4 (CONT.<sup>2</sup>)**

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```

      . . . . .
690 LYGQLLGSTSPGPGHYLRCDSTQPLLAGLTPSPKSYENLWFQASPLGTL 739
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
751 LYGQLLGSTSPGPGHYLRCDSTQPLLAGLTPSPKSYENLWFQASPLGTL 800
      . . . . .

      740 VTPAPSQEDDCVFGPLLNFPLLQGIRVHGMEALGSF 775
          | | | | | | | | | | | | | | | | | | | | | | | | | | | |
      801 VTPAPSQEDDCVFGPLLNFPLLQGIRVHGMEALGSF 836

```

FIG. 4 (CONT. <sup>3</sup>)



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MARLGNCSLTWAALIILLPGSLEECGHISVSAPIVHLGDPITASCIKQ 50  
|||||  
1 MARLGNCSLTWAALIILLPGSLEECGHISVSAPIVHLGDPITASCIKQ 50

51 NCSHLDPEPQILWRLGAELQPGGRQQRSLSDGTQESIITLPHLNHTQAFLS 100  
|||||  
51 NCSHLDPEPQILWRLGAELQPGGRQQRSLSDGTQESIITLPHLNHTQAFLS 100

101 CCLNWGNSLQILDQVELRAGYPPIAPHNLSCLMNLTTSSLICQWEPGPET 150  
|||||  
101 CCLNWGNSLQILDQVELRAGYPPIAPHNLSCLMNLTTSSLICQWEPGPET 150

151 HLPTSFTLKSFKSRGNCQTQGDSILDCVPKDGQSHCCIPRKHLLLYQNMG 200  
|||||  
151 HLPTSFTLKSFKSRGNCQTQGDSILDCVPKDGQSHCCIPRKHLLLYQNMG 200

201 IWVQAENALGTSMSPQLCLDPMDVVKLEPPMLRTMDPSPEAAPQAGCLQ 250  
|||||  
201 IWVQAENALGTSMSPQLCLDPMDVVKLEPPMLRTMDPSPEAAPQAGCLQ 250

FIG. 5







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1 MQKIMHISVLLSPVLWGLIFGVSSNSIQIGGLEPRGADQEYSAFRVGMVQ 50  
|||||  
1 MQKIMHISVLLSPVLWGLIFGVSSNSIQIGGLEPRGADQEYSAFRVGMVQ 50

51 FSTSEFRLTPHIDNLEVANSFAVTNAFCSQFSRGVYAI FGFYDKKSVNTI 100  
|||||  
51 FSTSEFRLTPHIDNLEVANSFAVTNAFCSQFSRGVYAI FGFYDKKSVNTI 100

101 TSFCGTLHVSFITPSFPTDGTGTHPFVIQMRPDLKGALLSLIEYYQWDKFAY 150  
|||||  
101 TSFCGTLHVSFITPSFPTDGTGTHPFVIQMRPDLKGALLSLIEYYQWDKFAY 150

151 LYDSDRGLSTLQAVLDSAAEKKWQVTAINVGNINNDKKDEMYRSLFQDLE 200  
|||||  
151 LYDSDRGLSTLQAVLDSAAEKKWQVTAINVGNINNDKKDEMYRSLFQDLE 200

201 LKKERRVILDCERDKVNDIVDQVITIGKHVKGYHYIIANLEFTDGDLLKI 250  
|||||  
201 LKKERRVILDCERDKVNDIVDQVITIGKHVKGYHYIIANLEFTDGDLLKI 250

FIG. 6



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```

451 AEIAKHCGFKYKLTIVGDGKYGARDADTKIWNMGVGVGELVYGKADIAIAPL 500
    | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
451 AEIAKHCGFKYKLTIVGDGKYGARDADTKIWNMGVGVGELVYGKADIAIAPL 500

501 TITLVREEVIDFSKPFMSLGIŠIMIKKPQKSKPGVFSFLDPLAYEIMCI 550
    | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
501 TITLVREEVIDFSKPFMSLGIŠIMIKKPQKSKPGVFSFLDPLAYEIMCI 550

551 VFAYIGVSVVFLVSRFSPYEWHTTEEFEDGRETQSSSESTNEFGIFNSLWF 600
    | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
551 VFAYIGVSVVFLVSRFSPYEWHTTEEFEDGRETQSSSESTNEFGIFNSLWF 600

601 SLGAFMRQGCDISPRSLSGRIVGGVWFFTLIIISSYTANLAAFLTVERM 650
    | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
601 SLGAFMRQGCDISPRSLSGRIVGGVWFFTLIIISSYTANLAAFLTVERM 650

651 VSPIESAEDLSKQTEIAYGTLDSGSTKEFFRRRSKIAVFDKMWTYMRSAEP 700
    | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
651 VSPIESAEDLSKQTEIAYGTLDSGSTKEFFRRRSKIAVFDKMWTYMRSAEP 700

```

FIG. 6 (CONT.<sup>2</sup>)

```

701 SVFVRTAEGVARVRKSKGYAYLLESTMNEYIEQRKPCDTMKVGGNLD 750
|||||
701 SVFVRTAEGVARVRKSKGYAYLLESTMNEYIEQRKPCDTMKVGGNLD 750

751 KGYGIATPKGSSLGTPVNLAVLKLSEQGVLDKLNKNWYDKGEXG 795
|||||
751 KGYGIATPKGSSLGTPVNLAVLKLSEQGVLDKLNKNWYDKGECG 795

```



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```

1 MKSIYFVAGLFVMLVQGSWQSLQDTEEKSRFSASQADPLSDPDQMNED 50
  |||||
1 MKSIYFVAGLFVMLVQGSWQSLQDTEEKSRFSASQADPLSDPDQMNED 50
  . . . . .
51 KRHSQGTFTSDYSKYLDSTRRAQDFVQWLMNTKRNRRNNIAKRHDEFERHAE 100
  |||||
51 KRHSQGTFTSDYSKYLDSTRRAQDFVQWLMNTKRNRRNNIAKRHDEFERHAE 100
  . . . . .
101 GTFTSVI.....FPEEVAIVEELGRRHADGS 126
  ||||| : |||||
101 GTFTSDVSSYLEGQAAKEFIAWLVKGRGRDRDFPEEVAIVEELGRRHADGS 150
  . . . . .
127 FSDEMNTISDNLAARDFINWLIQTKITDRK 156
  ||||| |||||
151 FSDEMNTILDNLAARDFINWLIQTKITDRK 180

```

FIG. 7

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```

6  SG TARK TLHF EISKEGSDL SVVERAEVWFLKVPKANRTRTKVTIRLFQQ 55
   |||||
129 SG TARK TLHF EISKEGSDL SVVERAEVWFLKVPKANRTRTKVTIRLFQQ 178
   |||||

56 QKHPQGS LDTGEEAEVGLKGERSELLSEKVVDARKSTWHVFPVSSSIQ 105
   |||||
179 QKHPQGS LDTGEEAEVGLKGERSELLSEKVVDARKSTWHVFPVSSSIQ 228
   |||||

106 RLDDQGS LDTVRIACEQCQESGASLVLLGKKKKKEEGEGKKGGEGG 155
   |||||
229 RLDDQGS LDTVRIACEQCQESGASLVLLGKKKKKEEGEGKKGGEGG 278
   |||||

156 AGADEEKEQSHRPFLMLQARQSEDPHRRRRRGLCDGKVNICCKKQFFV 205
   |||||
279 AGADEEKEQSHRPFLMLQARQSEDPHRRRRRGLCDGKVNICCKKQFFV 328
   |||||

```

FIG. 8

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206 SFKDIGWNDWIIAPSGYHANYCEGECPSHIAGTSGSSLSFHSTVINHYRM 255  
|||||  
329 SFKDIGWNDWIIAPSGYHANYCEGECPSHIAGTSGSSLSFHSTVINHYRM 378  
  
256 RGHSPFANLKSCCVPTKLRPMSMLYYDDGQNI IKKDIQNMIVEECGCS 303  
|||||  
379 RGHSPFANLKSCCVPTKLRPMSMLYYDDGQNI IKKDIQNMIVEECGCS 426

FIG. 8 (CONT.<sup>1</sup>)

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```

1 MNSFSTSAFGPVAFSLGLLLVLPAAFPAPVPPGEDSKDVAAPHRQPLTSS 50
  |||||
1 MNSFSTSAFGPVAFSLGLLLVLPAAFPAPVPPGEDSKDVAAPHRQPLTSS 50
  |||||

51 ERIDKQIRYILDGISAIRKETCNXSNMC.....EKDG 82
  |||||

51 ERIDKQIRYILDGISAIRKETCNKSNMCESSEKEALAENNLNLPKMAEKDG 100
  |||||

83 CFQSGFNEETCLVKIITGLLEFEVYLEYLQNRFESEEEQARAVQMSTKVL 132
  |||||

101 CFQSGFNEETCLVKIITGLLEFEVYLEYLQNRFESEEEQARAVQMSTKVL 150
  |||||

133 IQFLQKKAKNLDAITTPDPPTTNASLLTKLQAQNLQDQMTTHLILRSFKE 182
  |||||

151 IQFLQKKAKNLDAITTPDPPTTNASLLTKLQAQNLQDQMTTHLILRSFKE 200
  |||||

183 FLQSSLRALRQM 194
  |||||

201 FLQSSLRALRQM 212

```

FIG. 9

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```

1 MNSFST..... 6
  |||||
1 MNSFSTAAGPVAFSLGLLVLPAAFPAPVPPGEDSKDVAAPHRQPLTSS 50
  .
7 .....TCNKSNMCESSKEALAEANNLNLPKMAEKDG 36
  .
  |||||
51 ERIDKQIRYILDGISA LRKETCNKSNMCESSKEALAEANNLNLPKMAEKDG 100
  .
  .
37 CFQSGFNEETCLVKIITGLLEFEVYLEYLQNRFESEEQARAVQMSTKVL 86
  |||||
101 CFQSGFNEETCLVKIITGLLEFEVYLEYLQNRFESEEQARAVQMSTKVL 150
  .
  .
87 IQFLQKKAKNLDAITTPDPPTNASLLTKLQANQWLQDMTTHLILRSFKE 136
  |||||
151 IQFLQKKAKNLDAITTPDPPTNASLLTKLQANQWLQDMTTHLILRSFKE 200
  .
  .
137 FLQSSLRALRQM 148
  |||||
201 FLQSSLRALRQM 212

```

FIG. 10

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```

1  MPRLEFHLLEFCLLNQFSRAVAACKWKDDVIKLCGRELVRAQIAICGMS  50
   |||||
1  MPRLEFHLLEFCLLNQFSRAVAACKWKDDVIKLCGRELVRAQIAICGMS  50

51  TWSKRSLSQEDAPQTPRPVAAGDFIQTVSLGISPDGGKALRTGSCFTREF 100
   |||||
51  TWSKRSLSQEDAPQTPRPVA..... 70

101 LGALSKLVPSFINKDTETIIIMLEFIANLPPELKAALSERQPSLPQLQY 150
   .:|||||
71.... EIVPSFINKDTETIIIMLEFIANLPPELKAALSERQPSLPQLQY 115

151 VPALKDSSLLFEEFKKLIRNRQSEAADSNPSELKYLGLDTHSQKKRRPYV 200
   |||||. | |||||
116 VPALKDSNLSFEEFKKLIRNRQSEAADSNPSELKYLGLDTHSQKKRRPYV 165

201 ALFEKCCCLIGCTKRSLAKYC 220
   |||||
166 ALFEKCCCLIGCTKRSLAKYC 185

```

FIG. 11

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1 MKLCVTVLSLLMLVAAFCSPALSAPMGSDPPTACCFSTARKLPRNFVVD 50  
|||||  
1 MKLCVTVLSLLMLVAAFCSPALSAPMGSDPPTACCFSTARKLPRNFVVD 50  
51 YYETSSLCSQPAVV...GKQVCADPSESWSVQYVYDLELN 87  
|||||  
51 YYETSSLCSQPAVVFTKRSKQVCADPSESWSVQYVYDLELN 92

FIG. 12

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```

1  MGLAWGLGVFLMHVCGTNRIPESGGDNVFDIFELTGAARKGSGRRLVK  50
  |||||
1  MGLAWGLGVFLMHVCGTNRIPESGGDNVFDIFELTGAARKGSGRRLVK  50

51  GPDSPSPAFRIEDANLIPVPDDKFQDLVDVRAEKGFLLLASLRQMKT  100
  |||||
51  GPDSPSPAFRIEDANLIPVPDDKFQDLVDVRAEKGFLLLASLRQMKT  100

101  RGTLLALERKDHSGQVFSVSNKGAGTLDLSLTVQGKHVSVSEALLAT  150
  |||||
101  RGTLLALERKDHSGQVFSVSNKGAGTLDLSLTVQGKHVSVSEALLAT  150

151  GQWKSITLQVQEDRAQLYIDCEKMEAEALDVPIQSVFTRDLASIALRIA  200
  |||||
151  GQWKSITLQVQEDRAQLYIDCEKMEAEALDVPIQSVFTRDLASIALRIA  200

201  KGGVNDNFQGVLQNVRFVFGTTPEDILRNKGCSSSTSVLLTLDNNVVNGS  250
  |||||
201  KGGVNDNFQGVLQNVRFVFGTTPEDILRNKGCSSSTSVLLTLDNNVVNGS  250

```

FIG. 13



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251	SPAIR	NYIGHKTKDLQAICGISCDELSSMVLELRGLRTIVTTLQDSIRK	300
251	SPAIR	NYIGHKTKDLQAICGISCDELSSMVLELRGLRTIVTTLQDSIRK	300
301	VTEEN	KELANELRRPPLCYHNGVQYRNNEEWTVDSCTECHCQNSVTICKK	350
301	VTEEN	KELANELRRPPLCYHNGVQYRNNEEWTVDSCTECHCQNSVTICKK	350
351	VSCP	IMPCSNATVPDGECCPRCWPSPDSADDGWSPSEWTSCTSCGNGIQ	400
351	VSCP	IMPCSNATVPDGECCPRCWPSPDSADDGWSPSEWTSCTSCGNGIQ	400
401	QRGR	SCDSLNNRCEGSSVQTRTCHIQCCKRFRKQDGGWSHPWSSCSVT	450
401	QRGR	SCDSLNNRCEGSSVQTRTCHIQCCKRFRKQDGGWSHPWSSCSVT	450
451	CGDG	VITRILCNPSPPQMNGKPCGEARETKACKKDACPINGGWPWSP	500
451	CGDG	VITRILCNPSPPQMNGKPCGEARETKACKKDACPINGGWPWSP	500

**FIG. 13 (CONT.)<sup>1</sup>**

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```

      .      .      .      .      .
501 WDICSVTGGGVQKRSRLCENNPTPQFGGKDCVGDVTENQICNKQDCPIDG 550
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
501 WDICSVTGGGVQKRSRLCENNPTPQFGGKDCVGDVTENQICNKQDCPIDG 550

      .      .      .      .      .
551 CLSNPCFAGVKCTSYPDGSWKCGACPPGYSGNGIQCTDVDECKEVPDADF 600
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
551 CLSNPCFAGVKCTSYPDGSWKCGACPPGYSGNGIQCTDVDECKEVPDADF 600

      .      .      .      .      .
601 NHNGEHCENTDPGYNCLPCPPRFTGSQPFQGVGEHATANKQVCKPRNPC 650
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
601 NHNGEHCENTDPGYNCLPCPPRFTGSQPFQGVGEHATANKQVCKPRNPC 650

      .      .      .      .      .
651 TDGTHDCNKNACNYLGHYSDEMPYRCECKPGYAGNGIICGEDTDLDGWPN 700
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
651 TDGTHDCNKNACNYLGHYSDEMPYRCECKPGYAGNGIICGEDTDLDGWPN 700

      .      .
701 ENLVCVANATYHCKKDNCPNLP 722
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
701 ENLVCVANATYHCKKDNCPNLP 722

```

FIG. 13 (CONT.<sup>2</sup>)

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```

1  MGLAWGLGVLFMLHVCGTNRIPESGGDNSVFEDIFELTGAARKGSGRRLLVK  50
   |||||
1  MGLAWGLGVLFMLHVCGTNRIPESGGDNSVFEDIFELTGAARKGSGRRLLVK  50

51  GPDSSPAFRIEDANLIPVPDDKFFQDLVDVRAEKGFLLLASLRQMKKT  100
   |||||
51  GPDSSPAFRIEDANLIPVPDDKFFQDLVDVRAEKGFLLLASLRQMKKT  100

101  RGTLALERKDHSGQVFSVSNKGAGTLDLSLTVQKGQHVVSVVEEALLAT  150
   |||||
101  RGTLALERKDHSGQVFSVSNKGAGTLDLSLTVQKGQHVVSVVEEALLAT  150

151  GQWKSITLFVQEDRAQLYIDCEKMENAEILDVPIQSVFTRDLASIALRIA  200
   |||||
151  GQWKSITLFVQEDRAQLYIDCEKMENAEILDVPIQSVFTRDLASIALRIA  200

201  KGGVNDNFQGVLQNVRFVFGTTPEDILRNKGCSSSTSVLLTLDNNVVNGS  250
   |||||
201  KGGVNDNFQGVLQNVRFVFGTTPEDILRNKGCSSSTSVLLTLDNNVVNGS  250

```

FIG. 14

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251	SPAIR	NYIGHKTKDLQAICGIS	DELSSMVLELRGLRTIV	TLQDSIRK	300
251	SPAIR	NYIGHKTKDLQAICGIS	DELSSMVLELRGLRTIV	TLQDSIRK	300
301	VTEEN	KELANELRRPPLCYHN	GVQYRNNEE	WTVDSCTECHCQNSVTICKK	350
301	VTEEN	KELANELRRPPLCYHN	GVQYRNNEE	WTVDSCTECHCQNSVTICKK	350
351	VSCP	IMPCSNATVPDGECCPR	WPSDSAD	DGSPSEWTS	CSCTSCGNGIQ 400
351	VSCP	IMPCSNATVPDGECCPR	WPSDSAD	DGSPSEWTS	CSCTSCGNGIQ 400
401	QRGR	SCDSLNNRCEGSSVQ	TRTCHIQE	CDKRFKQDGGWSHSPWSSCSVT	450
401	QRGR	SCDSLNNRCEGSSVQ	TRTCHIQE	CDKRFKQDGGWSHSPWSSCSVT	450
451	CGDG	VITRILCN	SPSPQMNGKPC	EGEARETKACKKD	ACPINGGWGPWSP 500
451	CGDG	VITRILCN	SPSPQMNGKPC	EGEARETKACKKD	ACPINGGWGPWSP 500

**FIG. 14 (CONT.)**



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```

1  MGLAWGLGVLFMLHVCGTNRIPESGGDNSVFDIFELTGAARKSGRRLLVK  50
   ||||||||||||||||||||||||||||||||||||||||||||||||
1  MGLAWGLGVLFMLHVCGTNRIPESGGDNSVFDIFELTGAARKSGRRLLVK  50

51  GPDSSPAFRIEDANLIPVPDDKFDQLVDAVRAEKGFLLASLRQMKKT  100
   ||||||||||||||||||||||||||||||||||||||||||||||||
51  GPDSSPAFRIEDANLIPVPDDKFDQLVDAVRTEKGFLLASLRQMKKT  100

101  RGTLLALERKDHSGQVFSVSNKGAGTLDLSLTVQKQHVVSVEEALLAT  150
   ||||||||||||||||||||||||||||||||||||||||||||||||
101  RGTLLALERKDHSGQVFSVSNKGAGTLDLSLTVQKQHVVSVEEALLAT  150

151  GQWKSITLFVQEDRAQLYIDCEKMENAEILDVPIQSVFTRDLASIALRIA  200
   ||||||||||||||||||||||||||||||||||||||||||||||||
151  GQWKSITLFVQEDRAQLYIDCEKMENAEILDVPIQSVFTRDLASIALRIA  200

201  KGGVNDNFQGVLFQNVRFVFGTTPEDILRNKGCSSSTSVLLTLDNNVVNGS  250
   ||||||||||||||||||||||||||||||||||||||||||||||||
201  KGGVNDNFQGVLFQNVRFVFGTTPEDILRNKGCSSSTSVLLTLDNNVVNGS  250

```

FIG. 15

```

251 SPAIRTYIGHKTKDLQAICGISCDLSMVLRLGLRTIVTTLQDSIRK 300
|||||
251 SPAIRTYIGHKTKDLQAICGISCDLSMVLRLGLRTIVTTLQDSIRK 300

301 VTEENKELANELRRPPLCYHNGVQYRNNEEWTVDSCTECHCQNSVTICKK 350
|||||
301 VTEENKELANELRRPPLCYHNGVQYRNNEEWTVDSCTECHCQNSVTICKK 350

351 VSCPIMPCSNATVPDGECCPRCWPSADSADGWSPWSEWTSCTSCGNGIQ 400
|||||
351 VSCPIMPCSNATVPDGECCPRCWPSADSADGWSPWSEWTSCTSCGNGIQ 400

401 QGRSCDSLNNRCEGSSVQTRTCHIQECDKRFKQDGGWSHWSPWSSCSVT 450
|||||
401 QGRSCDSLNNRCEGSSVQTRTCHIQECDKRFKQDGGWSHWSPWSSCSVT 450

451 CGDGVITRIRLNCNSPSPQMNGKPCGEARETKACKKDACP 490
|||||
451 CGDGVITRIRLNCNSPSPQMNGKPCGEARETKACKKDACP 490

```

**FIG. 15 (CONT.)<sup>1</sup>**

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```

1  MGLAWGLGVLFMLHVCGTNRIPESGGDNSVFDFELTGAARKGSGRRLVK  50
  |||||
1  MGLAWGLGVLFMLHVCGTNRIPESGGDNSVFDFELTGAARKGSGRRLVK  50

51  GPDSSPAFRIEDANLIPVPDDKFQDLVDVRAEKGFLLASLRQMKT  100
  |||||
51  GPDSSPAFRIEDANLIPVPDDKFQDLVDVRAEKGFLLASLRQMKT  100

101  RGTLLALERKDHSGQVFSVNSNGKAGTLDLSLTQVGKQHVSVVEEALLAT  150
  |||||
101  RGTLLALERKDHSGQVFSVNSNGKAGTLDLSLTQVGKQHVSVVEEALLAT  150

151  GQWKSITLQVQEDRAQLYIDCEKMENAEILDVPIQSVFTRDLASIALRIA  200
  |||||
151  GQWKSITLQVQEDRAQLYIDCEKMENAEILDVPIQSVFTRDLASIALRIA  200

201  KGGVNDNFQGVLQNVRFVFGTTPEDILRNKGCSSSTSVLLTLDNNVVNGS  250
  |||||
201  KGGVNDNFQGVLQNVRFVFGTTPEDILRNKGCSSSTSVLLTLDNNVVNGS  250

```

FIG. 16



**SHRSTITIIE SHEET (RIIE 26)**

```

251 SPAIRTYIGHKTKDLQAICGISDELSSMVLELRGLRTIVTTLQDSIRK 300
|||||
251 SPAIRTYIGHKTKDLQAICGISDELSSMVLELRGLRTIVTTLQDSIRK 300
|||||
301 VTEENKELANELRRPPLCYHNGVQYRNNEEWTVDSCTECHCQNSVTICKK 350
|||||
301 VTEENKELANELRRPPLCYHNGVQYRNNEEWTVDSCTECHCQNSVTICKK 350
|||||
351 VSCPIMPCSNATVPDGECCPRCWPSADSADDGWSPSEWTSCTSCGNGIQ 400
|||||
351 VSCPIMPCSNATVPDGECCPRCWPSADSADDGWSPSEWTSCTSCGNGIQ 400
|||||
401 QGRSCDSLNNRCEGSSVQTRTCHIQECDKRCKHLSLGTW 441
|||||
401 QGRSCDSLNNRCEGSSVQTRTCHIQECDKRFKQ...DGGW 438

```

FIG. 16 (CONT.)<sup>1</sup>

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```

1  MAALMTPGTGAPPAPGDFSGEGSQGLPDPSPPEPKQLPELIRMKRDGGRLS  50
   |||||
1  MAALMTPGTGAPPAPGDFSGEGSQGLPDPSPPEPKQLPELIRMKRDGGRLS  50
   |||||

51  EADIRGFVAAVVNGSAQGAQIGAMLMAIRLRGMDLEETSVLTQALAQSGQ  100
   |||||
51  EADIRGFVAAVVNGSAQGAQIGAMLMAIRLRGMDLEETSVLTQALAQSGQ  100
   |||||

101 QLEWPEAWRQQLVDKHKSTGGVGDKVSLVLAPALACGCKVPMISGRGLGH  150
   |||||
101 QLEWPEAWRQQLVDKHKSTGGVGDKVSLVLAPALACGCKVPMISGRGLGH  150
   |||||

151 TGGTLDKLESI PGFNVIQSPEQMQLLDQAGCCIVGQSEQLVPADGILYA  200
   |||||
151 TGGTLDKLESI PGFNVIQSPEQMQLLDQAGCCIVGQSEQLVPADGILYA  200
   |||||

201 ARDVTATVDSLPLITASILSKKLVEGLSALVVDVKFGGAAVFPNQEQAARE  250
   |||||
201 ARDVTATVDSLPLITASILSKKLVEGLSALVVDVKFGGAAVFPNQEQAARE  250
   |||||

```

FIG. 17

RESTITUTE SHEET (RULE 26)

**FIG. 17 (CONT.<sup>1</sup>)**

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```

1 MAALMTPGTGAPPAPGDFSGEGSQGLPDPSPPEPKQLPELIRMKRDGGRLS 50
  |||||
1 MAALMTPGTGAPPAPGDFSGEGSQGLPDPSPPEPKQLPELIRMKRDGGRLS 50

51 EADIRGFVAAVNGSAQGAQIGAMLMAIRLRGMDLEETSVLTQALAQSGQ 100
  |||||
51 EADIRGFVAAVNGSAQGAQIGAMLMAIRLRGMDLEETSVLTQALAQSGQ 100

101 QLEWPEAWRQQQLVDKHSSTGGVGDKVSLVLAPALAAACGCKVPMISGRGLGH 150
  |||||
101 QLEWPEAWRQQQLVDKHSSTGGVGDKVSLVLAPALAAACGCKVPMISGRGLGH 150

151 TGGTLDKLESIPGFNVIQSPEQMQLLDQAGCCIVGQSEQLVPADGILYA 200
  |||||
151 TGGTLDKLESIPGFNVIQSPEQMQLLDQAGCCIVGQSEQLVPADGILYA 200

201 ARDVTATVDSLPLIT.....G.....WRG.SQ..P....R 223
  |||||
201 ARDVTATVDSLPLITASILSKKLVEGLSALVVDVKF.GGAAVFPNQEQAR 249
  .

```

FIG. 18





[illegible]FIG. 19 (CONT.<sup>1</sup>)

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```

1 MASRLTLTLLLLLAGDRASSNP NATSS.....VI 31
  ||||| ||||| ||||| ||||| |||||
1 MASRLTLTLLLLLAGDRASSNP NATSSSSQDPESLQDRGEGKVATTVI 50

32 SKMLFEVEPILEVSSLPTNSTNSATKITANTTDEPTTQPTTEPTTQPTI 81
  ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
51 SKMLFEVEPILEVSSLPTNSTNSTNSATKITANTTDEPTTQPTTEPTTQPTI 100

82 QPTQPTTQLPTDSPTQPTTGSCFCPGPVTLCSDLESHTAEVLGDALVDFS 131
  ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
101 QPTQPTTQLPTDSPTQPTTGSCFCPGPVTLCSDLESHTAEVLGDALVDFS 150

132 LKLYHAFSAMKKVETNMAFSPFSIASLLTQVLLGAGENTKTNLESILSYP 181
  ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
151 LKLYHAFSAMKKVETNMAFSPFSIASLLTQVLLGAGENTKTNLESILSYP 200

182 KDFTCVHQALKGETTKGVTSVSQIFHSPDLAIRDTFVNASRTLYSSSPRV 231
  ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
201 KDFTCVHQALKGETTKGVTSVSQIFHSPDLAIRDTFVNASRTLYSSSPRV 250

```

FIG. 20

ALBERTVILLE DISTRICT / BULL FIGHT



**FIG. 20 (CONT.<sup>1</sup>)**

```

1  MMDEEEVSLPRFKLEESYDMESVLRNLGMTDAFELGKADFSGMSQTDL 50
   |||||
261 MMDEEEVSLPRFKLEESYDMESVLRNLGMTDAFELGKADFSGMSQTDL 310
   |||||

   . . .
51  SLSKVVKHSFVEVNEEGTEAAAAATAAIMMRCARFVPRFCADHPFLFFIQ 100
   |||||
311 SLSKVVKHSFVEVNEEGTEAAAAATAAIMMRCARFVPRFCADHPFLFFIQ 360
   |||||

   .
101 HSKTNGILFCGRFSSP 116
   | |||||
361 HRKTNGILFCGRFSSP 376

```

**FIG. 21**



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```

251 EKFEWTRLDMMDEEEV..... 267
      |||||||
251 EKFEWTRLDMMDEEEVSLPRFKLEESYDMESVLRNLGMTDAFELGKA 300

268 .....EEGTEAAAAATAAIMMMRCARFVPRFC 293
      |||||||
301 DFSGMSQTDLSLSKVHKSFEVNEEGTEAAAAATAAIMMMRCARFVPRFC 350

294 ADHPFLEFFIQHKTNGILFCGRFSSP 319
      |||||||
351 ADHPFLEFFIQHRKTNGILFCGRFSSP 376

```

FIG. 22 (CONT.<sup>1</sup>)

FIG. 23

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[illegible]

51 AQMAQ 55

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

51 AQMAQ 55

**FIG. 24**

ALPHABETIC LIST (REV. 5-65)

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**FIG. 25**

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83 MSAPAAKVSKKELNSNHDGADETSEKEQQAIEHIDEVQNEIDRLNEQAS 132  
|||||  
1 MSAPAAKVSKKELNSNHDGADETSEKEQQAIEHIDEVQNEIDRLNEQAS 50  
133 EEILKVEQKYNKLRQPPFFQKRSELIAKIPNFWVTTFVNHPQVSALLGEED 182  
|||||  
51 EEILKVEQKYNKLRQPPFFQKRSELIAKIPNFWVTTFVNHPQVSALLGEED 100  
183 EEALHYLTRVEVTEFFEDIKSGYRIDFYFDENPYFENKVLSEFHLNESGD 232  
|||||  
101 EEALHYLTRVEVTEFFEDIKSGYRIDFYFDENPYFENKVLSEFHLNESGD 150  
233 PSSKSTEIKWKSGKDLTKRSSQTQNKASRKQRQHEEPESFTWFTDHS DAG 282  
|||||  
151 PSSKSTEIKWKSGKDLTKRSSQTQNKASRKQRQHEEPESFTWFTDHS DAG 200  
283 ADELGEVIKDDIWP NPLQYYLVPDMDDEEGEGEEDDDDDDEEEGLE DIDE 332  
|||||  
201 ADELGEVIKDDIWP NPLQYYLVPDMDDEEGEGEEDDDDDDEEEGLE DIDE 250  
333 EGDEDEGEDEDDDEGEEGEEDGEDD 359  
|||||  
251 EGDEDEGEDEDDDEGEEGEEDGEDD 277

FIG. 26



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1 MSAPAAKVSKKELNSNHDGADETSEKEQQAIEHIDEVQNEIDRLNEQAS 50  
|||||  
1 MSAPAAKVSKKELNSNHDGADETSEKEQQAIEHIDEVQNEIDRLNEQAS 50  
51 EEILKVEQKYNKLRQPFQKRSELIAKIPNFWVTTFFVNHPQVSALLGEED 100  
|||||  
51 EEILKVEQKYNKLRQPFQKRSELIAKIPNFWVTTFFVNHPQVSALLGEED 100  
101 EEALHYLTRVEVTEFEDIKSGYRIDFYFDENPYFENKVLKSEFFHLNESGD 150  
|||||  
101 EEALHYLTRVEVTEFEDIKSGYRIDFYFDENPYFENKVLKSEFFHLNESGD 150  
151 PSSKSTEIKWKSCKDLTKRSSQTQNKASRKRQH EEPESFTWTDHSDAG 200  
|||||  
151 PSSKSTEIKWKSCKDLTKRSSQTQNKASRKRQH EEPESFTWTDHSDAG 200  
201 ADELGEVIKDDIWPNPLOYYLVPDMDDEEGEGEEDDDDEEEGLEIDE 250  
|||||  
201 ADELGEVIKDDIWPNPLOYYLVPDMDDEEGEGEEDDDDEEEGLEIDE 250  
251 EGDGGGG 257  
||| |  
251 EGDEDEG 257

FIG. 27

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121 MSDASLRSTMERLVARGTFPVLVRTSACRSFLGFPVDHEELSRELQARL 170  
|||||  
1 MSDASLRSTMERLVARGTFPVLVRTSACRSFLGFPVDHEELSRELQARL 50

171 AELNAEDQNRWDYDFQQDMPLRGPGRQLQWTEVSDSDSVPAFYRETVQI... 217  
|||||  
51 AELNAEDQNRWDYDFQQDMPLRGPGRQLQWTEVSDSDSVPAFYRETVQVGR 100

218 .....FFAKRKRSAPEKSSGSDVPAPCPSPSA 243  
|||||  
251 AAGTAAASANGAAIKKLSGPLISDFFAKRKRSAPEKSSGSDVPAPCPSPSA 300

244 APGVGSVEQTPRKRLR 279  
|||||  
301 APGVGSVEQTPRKRLR 316

FIG. 28

```

2 MTLRHLPIILLILSGELYAEKQCDFFTVENGRIAQYYTTFKSFYFPMS 51
  |||||
1 MTLRHLPIILLILSGELYAEKQCDFFTVENGRIAQYYTTFKSFYFPMS 50
52 VDKKLSFFCLAGYATESGKQEEQIRCTAEGWSPNPRCYKKCLKPDLRNGY 101
  |||||
51 VDKKLSFFCLAGYATESGKQEEQIRCTAEGWSPNPRCYKKCLKPDLRNGY 100
102 VSNDKVLYKLQERMSYGCSSGYKTTGGKDEEVVHCLSAGWSSQPSCKREQ 151
  |||||
101 VSNDKVLYKLQERMSYGCSSGYKTTGGKDEEVVHCLSAGWSSQPSCKREQ 150
152 ETCLAPELEHGNYSTTQRTFKVKDIAVYCTAGYYTTTGKQTGEAECQAN 201
  |||||
151 ETCLAPELEHGNYSTTQRTFKVKDIAVYCTAGYYTTTGKQTGEAECQAN 200
202 GWSLTPQCCKMLMCSSLRLIENGYFHPVKQTYEEGDVVQFFCHENYYLSGS 251
  |||||
201 GWSLTPQCCKMLMCSSLRLIENGYFHPVKQTYEEGDLVQFFCHENYYLSGS 250

```

**FIG. 29**



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502 ISAQCNRGDVRYPMCIRKESKGMCASPPVIRNGDIVSSAARTYENGSSVE 551  
|||||  
501 ISAQCNRGDVRYPMCIRKESKGMCASPPVIRNGDIVSSAARTYENGSSVE 550  
552 YRCFDNHFLQGSQNVYCVDGVTTPPSCLEP 582  
|||||  
551 YRCFDNHFLQGSQNVYCVDGVTTPPSCLEP 581

FIG. 29 (CONT.<sup>2</sup>)



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160 LSKEVTSLSNSTQAEVPDDDGTESSLVAEIMVSGMNYEDDCGPGCGSH 209  
|||||  
801 LSKEVTSLSNSTQAEVPDDDGTESSLVAEIMVSGMNYEDDCGPGCGSH 850  
210 ARCVSDGETAECQCLKGFARDGNLCSIDIECVLARSDCPSTSSRCINTEG 259  
|||||  
851 ARCVSDGETAECQCLKGFARDGNLCSIDIECVLARSDCPSTSSRCINTEG 900  
260 GYVCRCEGYEGDGISCFDIDECQRGAHNCAENAACTNTEGGYNCTCAGR 309  
|||||  
901 GYVCRCEGYEGDGISCFDIDECQRGAHNCAENAACTNTEGGYNCTCAGR 950  
310 PSSPGLSCPDPSTAPSLLGEDGHHLDRNSYPGCPSSYDGYCLNGGVCMHIE 359  
|||||  
951 PSSPGRSCPDPSTAPSLLGEDGHHLDRNSYPGCPSSYDGYCLNGGVCMHIE 1000  
360 SLDSYTCNCVIGYSGDRCQTRDLRWELRHAGYGQKHDIMVVAVCMVALV 409  
|||||  
1001 SLDSYTCNCVIGYSGDRCQTRDLRWELRHAGYGQKHDIMVVAVCMVALV 1050

FIG. 30 (CONT.<sup>1</sup>)





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```

1 MPWGRRPTWLLAFLLVFLKISILSVTAWQTGNCQPGPLERSERSGTCAG 50
  |||||
1 MPWGRRPTWLLAFLLVFLKISILSVTAWQTGNCQPGPLERSERSGTCAG 50
  . . . . .
51 PAPFLVFSQGKKSISRI..... 66
  |||||
51 PAPFLVFSQGKKSISRIDPDGTHHQQQLVVDAGISADMDIHYYKKERLYWVDV 100
  . . .
67 ..... WAIPSVIRVNKRTGQNRVRLQGSMLKPSSLVVVHPLAKPGADP 109
  |||||
701 DHLWVSDWAIPSVIRVNKRTGQNRVRLQGSMLKPSSLVVVHPLAKPGADP 750
  . . .
110 CLYRNGGCEHICQESLGTARCLCREGFVKAWDGKMCPLPDYPILSGENAD 159
  |||||
751 CLYRNGGCEHICQESLGTARCLCREGFVKAWDGKMCPLPDYPILSGENAD 800
  . . .

```

FIG. 31



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```

360 SLDSYTCNCVIGYSGDRCQT.....
      379
      |||||||
1001 SLDSYTCNCVIGYSGDRCQTRDLRWELRHAGYGQKHDIMVVAVCMVALV
      1050
      .
      .
      .
      .
380 .....PPSSDRGPEIEGNHSLPSYRPPVGPEKLSLQSANG 415
      |||||||
1151 PHIDGMGTGQSCWIPSSDRGPEIEGNHSLPSYRPPVGPEKLSLQSANG
      1200
      .
      416 SCHERAPDLPRQTEPVQ 432
      |||||||
      1201 SCHERAPDLPRQTEPVK 1217

```

FIG. 31 (CONT.<sup>2</sup>)

**FIG. 32**

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```

:      1 MPWRRPTWLLAFLV..... 17
      |||||
      1 MPWRRPTWLLAFLVFLKISILSVTAWQTGNCQPGPLERSERSGTCAG 50
      .
      .
      .
      .
      18 .....SAECQCLKGFARDGNLCSIDIECVLARSDCPSTSSRCINTEG 59
      .|||||
      851 ARCVSDGETAECQCLKGFARDGNLCSIDIECVLARSDCPSTSSRCINTEG 900
      .
      60 GYVCRCEGYEGDGISCFDIECQRGAHNCAENAACTNTEGGYNCTCAGR 109
      |||||
      901 GYVCRCEGYEGDGISCFDIECQRGAHNCAENAACTNTEGGYNCTCAGR 950
      .
      110 PSSPGLSCPDSTAPSLLGEDGHHLDRNSYPGCPSSYDGYCLNGVCMHIE 159
      |||||
      951 PSSPGRSCPDSTAPSLLGEDGHHLDRNSYPGCPSSYDGYCLNGVCMHIE 1000
      .
      .
      .
  
```

FIG. 33

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160 SLDSYTCNCVIGSGDRCQTRDLRWELRHAGYGQKHDIMVAVCMVALV 209  
|||||  
1001 SLDSYTCNCVIGSGDRCQTRDLRWELRHAGYGQKHDIMVAVCMVALV 1050  
210 LLLLLGMWGTYYYRTRKQLSNPPKPCDEPSGVS SSSGPDSSSGAAVASC 259  
|||||  
1051 LLLLLGMWGTYYYRTRKQLSNPPKPCDEPSGVS SSSGPDSSSGAAVASC 1100  
260 PQWFVVLEKHQDPKNGSLPADGTNGAVVDAGLSPLQLGSHLTSWRQK 309  
|||||  
1101 PQWFVVLEKHQDPKNGSLPADGTNGAVVDAGLSPLQLGSHLTSWRQK 1150  
310 PHIDGMGTGQSCWIPPSSDRGPQEIEGNHLSYRPPVGPEKLHSLQSANG 359  
|||||  
1151 PHIDGMGTGQSCWIPPSSDRGPQEIEGNHLSYRPPVGPEKLHSLQSANG 1200  
360 SCHERAPDLPRQTEPVQ 376  
|||||  
1201 SCHERAPDLPRQTEPVK 1217

FIG. 33 (CONT.<sup>1</sup>)

1 MPWGR..... 5  
 |||||  
 1 MPWGRPTWLLAFLLVFLKISILSVTAWQTGNCQPGPLERSERSGTCAG 50

6 ..... KAWDGKMCLPQDYPILSGENAD 27  
 |||||  
 751 CLYRNGGCEHICQESLGTARCLCREGFVKAWDGKMCLPQDYPILSGENAD 800

28 LSKEVTSLSNSTQAEVPDDDGTESSLVAEIMVSGMNYEDDCGPGCGSH 77  
 |||||  
 801 LSKEVTSLSNSTQAEVPDDDGTESSLVAEIMVSGMNYEDDCGPGCGSH 850

78 ARCVSDGETAECQCLKGFARDGNLCSIDIECVLARSDCPSTSSRCINTEG 127  
 |||||  
 851 ARCVSDGETAECQCLKGFARDGNLCSIDIECVLARSDCPSTSSRCINTEG 900

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FIG. 34

128 GYVCRCEGYEGDGI SCFDI DECQ RGAHNCAENAACTNTEGGYNCTCAGR 177  
|||||  
901 GYVCRCEGYEGDGI SCFDI DECQ RGAHNCAENAACTNTEGGYNCTCAGR 950  
178 PSSPGLSCPDSTAPSL LGEDGHHLDRNSYPGCPSSYDGYCLNGGVCMHIE 227  
|||||  
951 PSSPGRSCPDSTAPSL LGEDGHHLDRNSYPGCPSSYDGYCLNGGVCMHIE 1000  
228 SLDSYTCNCVIGYSGDRCQTRDLRWELRHAGYGQKHDIMVVAVCMVALV 277  
|||||  
1001 SLDSYTCNCVIGYSGDRCQTRDLRWELRHAGYGQKHDIMVVAVCMVALV 1050  
278 LLLLLGMWGTYYYRTRKQLSNPPKNPCDEPSGVS SSGPDSSSGAAVASC 327  
|||||  
1051 LLLLLGMWGTYYYRTRKQLSNPPKNPCDEPSGVS SSGPDSSSGAAVASC 1100  
328 PQPWFVVLEKHQDPKNGSLPADGTNGAVVDAGLSPLQLGSHLT SWRQK 377  
|||||  
1101 PQPWFVVLEKHQDPKNGSLPADGTNGAVVDAGLSPLQLGSHLT SWRQK 1150

FIG. 34 (CONT.<sup>1</sup>)



FIG. 34 (CONT.<sup>2</sup>)

1 MFRELNEALELKDAHAATEESGDSRAHSSYLKTKKGQSTSRHKKTMVKKVG 50  
|||||  
337 MFRELNEALELKDAHAATEESGDSRAHSSYLKTKKGQSTSRHKKTMVKKVG 386

51 PDSD 54  
;  
||||  
387 PDSD 390

FIG. 35

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1 MKYPVWPRYSASLQPVVDSRHLTVATLEERPFIIVESPDGPGTGGCVPNTV 50  
|||||  
382 MKYPVWPRYSASLQPVVDSRHLTVATLEERPFIIVESPDGPGTGGCVPNTV 431  
51 PCRRQSNHTFSSGDVAPYTKLCKGFCIDILKKLARVVKFSYDLYLVTNG 100  
|||||  
432 PCRRQSNHTFSSGDVAPYTKLCKGFCIDILKKLARVVKFSYDLYLVTNG 481  
101 KHGKRVRGVWNGMIGEVYKRADMAIGSLTINEERSEIVDFSVPFVETGI 150  
|||||  
482 KHGKRVRGVWNGMIGEVYKRADMAIGSLTINEERSEIVDFSVPFVETGI 531  
151 SVMVARSNGTVSPSAFLEPYSPAVWMMFVMCLTVVAITVFMFEYFSPVS 200  
|||||  
532 SVMVARSNGTVSPSAFLEPYSPAVWMMFVMCLTVVAITVFMFEYFSPVS 581  
201 YNQNLTRGKKSGGPAFTIGKSVWLLWALVFNNNSVPIENPRGTTSKIMVLV 250  
|||||  
582 YNQNLTRGKKSGGPAFTIGKSVWLLWALVFNNNSVPIENPRGTTSKIMVLV 631  
.

FIG. 36

3

FIG. 36 (CONT.<sup>1</sup>)

501 PDLTASSAQASVLKMLQAARDMVTTAGVSSSLDRATRTIENWGGRRAPP 550  
 |||||  
 882 PDLTASSAQASVLKMLQAARDMVTTAGVSSSLDRATRTIENWGGRRAPP 931  
 .  
 551 PSPCPTPRSGSPCLPTPDRPEPSPTGWGPPDGGRAALVRRAPQPPGRP 600  
 |||||  
 932 PSPCPTPRSGSPCLPTPDRPEPSPTGWGPPDGGRAALVRRAPQPPGRP 981  
 .  
 601 PTPGPPLSDVSRVSRPFAWEARWPVRTGHCGRHLSASERPLSPARCHYSS 650  
 |||||  
 982 PTPGPPLSDVSRVSRPFAWEARWPVRTGHCGRHLSASERPLSPARCHYSS 1031  
 .  
 651 FPRADRSGRPFLLPFPEPPELEDLPLLGPQLARREALLHAAWARGSRPR 700  
 |||||  
 1032 FPRADRSGRPFLLF...PELEDLPLLGPQLARREALLHAAWARGSRPR 1078  
 .  
 701 HASLPSSVAEAFARPSSLPAGCTGPACARPDGHSACRRLAQAQSMCLPIY 750  
 |||||  
 1079 HASLPSSVAEAFARPSSLPAGCTGPACARPDGHSACRRLAQAQSMCLPIY 1128  
 .

FIG. 36 (CONT.<sup>2</sup>)

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```

751 REACQEGEQAGAPAWQHRQHVCLHAHAHLPCWGA VCPHLPPCASHGWL 800
      |||||
1129 REACQEGEQAGAPAWQHRQHVCLHAHAHLPCWGA VCPHLPPCASHGWL 1178
      |||||

801 SGAWGPLGHRGRTLGLGTGYRDSGGLDEISXVARGTQGFPGPCTWRRISS 850
      |||||
1179 SGAWGPLGHRGRTLGLGTGYRDSGGLDEISRVARGTQGFPGPCTWRRISS 1228
      |||||

      851 LESEV 855
      |||||
      1229 LESEV 1233

```

FIG. 36 (CONT.<sup>3</sup>)

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```

1 1 MRLAVGALLVCAVLGLCLAVPDKTVRWCAVSEHEATKCQSFDRHMKSVIP 50
  |||||
1 1 MRLAVGALLVCAVLGLCLAVPDKTVRWCAVSEHEATKCQSFDRHMKSVIP 50

51 SDGPSVACVKKASYLDCIRAIANEADAVTLDAGLVYDAYLAPNNLKPVV 100
  |||||
51 SDGPSVACVKKASYLDCIRAIANEADAVTLDAGLVYDAYLAPNNLKPVV 100

101 AEFYGSKEDPQTFYYAVAVVKKDSGFQMNQLRGKKSCHTGLGRSAGWNIP 150
  |||||
101 AEFYGSKEDPQTFYYAVAVVKKDSGFQMNQLRGKKSCHTGLGRSAGWNIP 150

151 IGLLYCDLPEPRKPLEKAVANFFSGSCAPCADGTDFFPQLCQLCPGCGCST 200
  |||||
151 IGLLYCDLPEPRKPLEKAVANFFSGSCAPCADGTDFFPQLCQLCPGCGCST 200

201 LNQYFGYSGAFKCLKDGAGDVAFVKHSTIFENLANKADRQYELLCLDNT 250
  |||||
201 LNQYFGYSGAFKCLKDGAGDVAFVKHSTIFENLANKADRQYELLCLDNT 250

```

FIG. 37

251 RKPVDEYKDCHLAQVPSHTTVVARSMGKEDLIWELNQAQEHFGKDKSKE 300  
 |||||  
 251 RKPVDEYKDCHLAQVPSHTTVVARSMGKEDLIWELNQAQEHFGKDKSKE 300  
 |||||  
 301 FQLFSSPHGKDLLFKDSAAGFLKVPPRMDAKMYLGYEYVTAIRNLREGTC 350  
 |||||  
 301 FQLFSSPHGKDLLFKDSAAGFLKVPPRMDAKMYLGYEYVTAIRNLREGTC 350  
 |||||  
 351 PEPTDECKPVKWCALSHHERLKCDEWSVNSVGKIECVSAETTEDCIAKI 400  
 |||||  
 351 PEPTDECKPVKWCALSHHERLKCDEWSVNSVGKIECVSAETTEDCIAKI 400  
 |||||  
 401 MNGEADAMSLDGGFVYIAGKCGLVPVLAENYNKSDNCEDTPEAGYFAVAV 450  
 |||||  
 401 MNGEADAMSLDGGFVYIAGKCGLVPVLAENYNKSDNCEDTPEAGYFAVAV 450  
 |||||  
 451 VKKSASDLTWDNLKGKKSCHTAFGRTAGWNIPMGLLYNKINHCRFDEFFS 500  
 |||||  
 451 VKKSASDLTWDNLKGKKSCHTAFGRTAGWNIPMGLLYNKINHCRFDEFFS 500  
 |||||

FIG. 37 (CONT.<sup>1</sup>)



501 EGCAPGSKKDSLCKLCMGSLNLCEPNNKEGYGYTGAFRCCLVEKGDVA 550  
|||||  
501 EGCAPGSKKDSLCKLCMGSLNLCEPNNKEGYGYTGAFRCCLVEKGDVA 550  
|||||  
551 FVKHQTVPQNTGGKNPDPWAKNLNEKDYELLCLDGTGTRKPVVEEYANCHLAR 600  
|||||  
551 FVKHQTVPQNTGGKNPDPWAKNLNEKDYELLCLDGTGTRKPVVEEYANCHLAR 600  
|||||  
601 APNHAVVTRKDKACVHKILRQQQLFGSNVTDCSGNFCFLRSETKDLF 650  
|||||  
601 APNHAVVTRKDKACVHKILRQQQLFGSNVTDCSGNFCFLRSETKDLF 650  
|||||  
651 RDDT.....H.....LLEACTFRRP 665  
||| |  
651 RDDTVCLAKLHDRNTYEKYLGEYVKAVGNLRKCSLLEACTFRRP 698

FIG. 37 (CONT.<sup>2</sup>)

1	MRLAVGALLVCAVLGLCLAVPDKTVRWCAVSEHEATKCQSF	RDHMKSVIP	50
1	MRLAVGALLVCAVLGLCLAVPDKTVRWCAVSEHEATKCQSF	RDHMKSVIP	50
51	SDGPSVACVKKASYLDCIRAIANA	EADAVTLDAGLVYDAYLAPNNLKP	VV 100
51	SDGPSVACVKKASYLDCIRAIANA	EADAVTLDAGLVYDAYLAPNNLKP	VV 100
101	AEFYGSKEDPQTFYAYAVVKKDSGFQMNQLRGKK	SCHTGLGRSAGWNIP	150
101	AEFYGSKEDPQTFYAYAVVKKDSGFQMNQLRGKK	SCHTGLGRSAGWNIP	150
151	IGLLYCDLPEPRKPLEKAVANFFSGSCAPCADGTD	FPQLCQLCPGCGCST	200
151	IGLLYCDLPEPRKPLEKAVANFFSGSCAPCADGTD	FPQLCQLCPGCGCST	200
201	LNQYFGYSGAFKCLKDGAGDVA	FVKHSTIFENLANKADR	DQYELLCLDNT 250
201	LNQYFGYSGAFKCLKDGAGDVA	FVKHSTIFENLANKADR	DQYELLCLDNT 250

**FIG. 38**

FIG. 38 (CONT.<sup>1</sup>)

449 EGCAFGSKKDS LCKLCMGSGNLNLC EPNNKEGYGYTGAFRCLVEKGDVA 498  
 |||||  
 501 EGCAFGSKKDS LCKLCMGSGNLNLC EPNNKEGYGYTGAFRCLVEKGDVA 550  
 . . . . .  
 499 FVKHQTVPQNTGGKNPDPWAKNLNEKDYELLCLDGTGTRKPVVEEYANCHLAR 548  
 |||||  
 551 FVKHQTVPQNTGGKNPDPWAKNLNEKDYELLCLDGTGTRKPVVEEYANCHLAR 600  
 . . . . .  
 549 APNHAVVTRKDKEACVHKILRQQQHLFGSNVTDCSGNFC LFRSETKD LLF 598  
 |||||  
 601 APNHAVVTRKDKEACVHKILRQQQHLFGSNVTDCSGNFC LFRSETKD LLF 650  
 . . . . .  
 599 RDDTVCLAKLHDRNTYEKYLGE EYVKAVGNLRKCSTSS LLEACTFRRP 646  
 |||||  
 651 RDDTVCLAKLHDRNTYEKYLGE EYVKAVGNLRKCSTSS LLEACTFRRP 698

FIG. 38 (CONT.<sup>2</sup>)

```

1 MAEGEGGEDEIQFLRTEDEVVLQCIATIHKEQRKFCCLAEGGNRLCFL 50
  |||
1 MAEGEGGEDEIQFLRTEDEVVLQCIATIHKEQRKFCCLAEGGNRLCFL 50

51 EPTSEAKYIPPDLCVCNFCVLEQSLSVRALQEMLANGTENGEGGAAQGGGH 100
  |||
51 EPTSEAKYIPPDLCVCNFCVLEQSLSVRALQEMLANGTENGEGGAAQGGGH 100

101 RTLLYGHAVLLRHVSFGMYLTCLTTSRSQTDKLAFDVGLREHATGEACWW 150
  |||
101 RTLLYGHAVLLRHVSFGMYLTCLTTSRSQTDKLAFDVGLREHATGEACWW 150

151 TIHPASKORSEGEKVRIGDDLILVSVSSERYLHLSVSNNGNIQVDASFMQT 200
  |||
151 TIHPASKORSEGEKVRIGDDLILVSVSSERYLHLSVSNNGNIQVDASFMQT 200

201 LWNVHPTCSGSSIEEGYLLGGHVVRFLFHGHDECLTIPSTDQNDQSQRRIIF 250
  |||
201 LWNVHPTCSGSSIEEGYLLGGHVVRFLFHGHDECLTIPSTDQNDQSQRRIIF 250

```

FIG. 39

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```

251 YEAGGAGTRAXSLWRVEPLRISWGSNIRWGQAFRLRLTTGHY LALTED 300
    ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
251 YEAGGAGTRARSLWRVEPLRISWGSNIRWGQAFRLRLTTGHY LALTED 300

301 QGLILQDRAKSDTKSTAFSFRASKELKEKLDSSHKRDI EGMGVPEIKYGD 350
    ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
301 QGLILQDRAKSDTKSTAFSFRASKELKEKLDSSHKRDI EGMGVPEIKYGD 350

351 SVCFVQHIASGLWVTYKAQDAKTSRLGPLKRKVILHQEGHMD DGLTLQRC 400
    ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
351 SVCFVQHIASGLWVTYKAQDAKTSRLGPLKRKVILHQEGHMD DGLTLQRC 400

401 QREESQAARIIRNTTALFSQFVSGNNRTAAPITLPIEEVLQTLQD LIAFY 450
    ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
401 QREESQAARIIRNTTALFSQFVSGNNRTAAPITLPIEEVLQTLQD LIAFY 450

451 QPPEEEMRHEDKQNKLRSLKNRQNLFKEEGMLALV LNCIDRLNXVNSVAH 500
    ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||
451 QPPEEEMRHEDKQNKLRSLKNRQNLFKEEGMLALV LNCIDRLNVNSVAH 500

```

FIG. 39 (CONT.<sup>1</sup>)

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```

501 FAGIAREESGMAWKEILNLLYKLLAALIRGNRNCAQFSNNLDWLISKLD 550
|||||
501 FAGIAREESGMAWKEILNLLYKLLAALIRGNRNCAQFSNNLDWLISKLD 550

551 RLESSSGILEVLHCILTESP EALNLIAEGHIKSII SLLDKHGRNHKVLDI 600
|||||
551 RLESSSGILEVLHCILTESP EALNLIAEGHIKSII SLLDKHGRNHKVLDI 600

601 LCSLCLCNGVAVRANQNLCIDNLLPRRNLLQLTRLINDVTSIRPNIFLG V 650
|||||
601 LCSLCLCNGVAVRANQNLCIDNLLPRRNLLQLTRLINDVTSIRPNIFLG V 650

651 AEGSAQYKKWFELIIDQVDPFLTAEP THLRVGWASSSGYAPXPGGEGW 700
|||||
651 AEGSAQYKKWFELIIDQVDPFLTAEP THLRVGWASSSGYAPXPGGEGW 700

701 GGNGVGDDLYSYGFDGLHLWSGRIPRAVASXNQHLRSDDVVSCCL.DLG 749
|||||
701 GGNGVGDDLYSYGFDGLHLWSGRIPRAVASINQHLLRSDDVCKLLPGRP G 750

```

FIG. 39 (CONT.<sup>2</sup>)

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750 CPASHASMGSPCRGCLRNFTDGLFFPVMFSAGVKVFLMGGRHGEFK 799  
|||||  
751 CPASHASMGSPCRGCLRNFTDGLFFPVMFSAGVKVFLMGGRHGEFK 800  
|||||  
800 FLPPSGYAPCYEALLPKEKMRLEPVKEYKRDADGIRDLLGTTQFLSQASF 849  
|||||  
801 FLPPSGYAPCYEALLPKEKMRLEPVKEYKRDADGIRDLLGTTQFLSQASF 850  
|||||  
850 IPCPVDTSQVILPPHLEKIRDRLAENIHELWGMNKKIELGWTFGKIRDDNK 899  
|||||  
851 IPCPVDTSQVILPPHLEKIRDRLAENIHELWGMNKKIELGWTFGKIRDDNK 900  
|||||  
900 RQHPCLVEFSKLPETEKNYNLQMSTETLKTLLXLGCHIAHVNPAAEEDLK 949  
|||||  
901 RQHPCLVEFSKLPETEKNYNLQMSTETLKTLLTLGCHIAHVNPAAEEDLK 950  
|||||  
950 KVKLPKNYMSNGYKPAPLDLSDVKLLPPQEIIVDKLAENAHNVWAKDRI 999  
|||||  
951 KVKLPKNYMSNGYKPAPLDLSDVKLLPPQEIIVDKLAENAHNVWAKDRI 1000

FIG. 39 (CONT.<sup>3</sup>)



1000 KQGTYGIQQDLKNRNPRLVPYALLDERTKKSNRDSLREAVRTFVGYG 1049  
 |||||  
 1001 KQGTYGIQQDLKNRNPRLVPYALLDERTKKSNRDSLREAVRTFVGYG 1050  
 |||||  
 1050 NIEPSDQELADSAVEKVSIDKIRFFRVERSYXVRSGKWYFEFEVVTGGDM 1099  
 |||||  
 1051 NIEPSDQELADSAVEKVSIDKIRFFRVERSYXVRSGKWYFEFEVVTGGDM 1100  
 |||||  
 1100 RVGWARPGCRPDVELGADDQAFVFEGRGQRWHQSGYFGRTWQPGDVVG 1149  
 |||||  
 1101 RVGWARPGCRPDVELGADDQAFVFEGRGQRWHQSGYFGRTWQPGDVVG 1150  
 |||||  
 1150 CMINLDDASMIFTLNGELLITNKGSELAFAADYEIENG FVPI CCLGLSQIG 1199  
 |||||  
 1151 CMINLDDASMIFTLNGELLITNKGSELAFAADYEIENG FVPI CCLGLSQIG 1200  
 |||||  
 1200 RMNLGTDASTFKFYTMCGLQEGFEFFAVNMNRDVAMWFSKR LPTFVNVPK 1249  
 |||||  
 1201 RMNLGTDASTFKFYTMCGLQEGFEFFAVNMNRDVAMWFSKR LPTFVNVPK 1250

FIG. 39 (CONT. 4)

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1250 DPHIEVMRIDGTMDSPCLKVTHKTFGTQNSNADMIYCRLSMPVECHSS 1299  
|||||  
1251 DPHIEVMRIDGTMDSPCLKVTHKTFGTQNSNADMIYCRLSMPVECHSS 1300  
|||||  
1300 FSHSPCLDSEAFQKRKQMQEILSHTTTQCYAIRIFXGQDPSCVWVGWVT 1349  
|||||  
1301 FSHSPCLDSEAFQKRKQMQEILSHTTTQCYAIRIFGGQDPSCVWVGWVT 1350  
|||||  
1350 PDYHLYSEKFDLNKNCTVTTLGDERGRVHESVKRSNCYMWGGDIVASS 1399  
|||||  
1351 PDYHLYSEKFDLNKNCTVTTLGDERGRVHESVKRSNCYMWGGDIVASS 1400  
|||||  
1400 QRSNRSNVDLEIGCLVDLAMGMLSF SANGKELGTCYQVEPNTKVFFPAVFL 1449  
|||||  
1401 QRSNRSNVDLEIGCLVDLAMGMLSF SANGKELGTCYQVEPNTKVFFPAVFL 1450  
|||||  
1450 QPTSTSLFQFELGKLKNAMPLSAAIFRSEEXNPVPQCPRLDVQTIQPV L 1499  
|||||  
1451 QPTSTSLFQFELGKLKNAMPLSAAIFRSEEXNPVPQCPRLDVQTIQPV L 1500  
|||||

FIG. 39 (CONT.<sup>5</sup>)

```

. . . . .
1500 WSRMPNSFLKVETERVSRHGWVQCLEPLQMMALHIPEENRCVDILELC 1549
|||||
1501 WSRMPNSFLKVETERVSRHGWVQCLEPLQMMALHIPEENRCVDILELC 1550
. . . . .
1550 EQEDLMRFHYHTLRLYSACALGNSRVAYALCSHVDSLQLFYAIDNKYLP 1599
|||||
1551 EQEDLMRFHYHTLRLYSACALGNSRVAYALCSHVDSLQLFYAIDNKYLP 1600
. . . . .
1600 GLLRSGFYDLLISIHLSAKERKLMKNEYIIPITSTTRNICLFPDESKR 1649
|||||
1601 GLLRSGFYDLLISIHLSAKERKLMKNEYIIPITSTTRNICLFPDESKR 1650
. . . . .
1650 HGLPGVGLRTCLKPGFRFSTPCFVVTGEDHQKQSP EIPLES LRTKALSML 1699
|||||
1651 HGLPGVGLRTCLKPGFRFSTPCFVVTGEDHQKQSP EIPLES LRTKALSML 1700
. . . . .

```

FIG. 39 (CONT.<sup>6</sup>)

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```

1700 TEAVQCSGAHIRDPVGGSVFQFVPLKLTLLVMGVFDDDDVRQILL 1749
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
1701 TEAVQCSGAHIRDPVGGSVFQFVPLKLTLLVMGVFDDDDVRQILL 1750

      .
1750 IDPSVFGEHSAGTEEGAEKEEVTQVEEKAVEAGEKAGKEAPVKGLLQTRL 1799
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
1751 IDPSVFGEHSAGTEEGAEKEEVTQVEEKAVEAGEKAGKEAPVKGLLQTRL 1800

      .
1800 PESVKLQMCCELLSYLCDCELQHRVEAIVAFGDIYVSKLQANQKFRYNELM 1849
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
1801 PESVKLQMCCELLSYLCDCELQHRVEAIVAFGDIYVSKLQANQKFRYNELM 1850

      .
1850 QALNMSAALTARKTKEFRSPPEQINMLNLFQLGENCPCEEIREELYDF 1899
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
1851 QALNMSAALTARKTKEFRSPPEQINMLNLFQLGENCPCEEIREELYDF 1900

      .
1900 HEDLLHCGVPLEEEEEEDTSWTGKLCALVYKIKGPPKPEKEQPTEEE 1949
      | | | | | | | | | | | | | | | | | | | | | | | | | | | |
1901 HEDLLHCGVPLEEEEEEDTSWTGKLCALVYKIKGPPKPEKEQPTEEE 1950

```

FIG. 39 (CONT.)

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1950 ERCPTTLKELISQTMICWAQEDQIQDSELVRMMFNLLRRQYDSIGELLQA 1999  
|||||  
1951 ERCPTTLKELISQTMICWAQEDQIQDSELVRMMFNLLRRQYDSIGELLQA 2000  
|||||  
2000 LRKTYTISHTSVSDTINLLAALGQIRSLLSVRMGKEEELLMINGLGDIMN 2049  
|||||  
2001 LRKTYTISHTSVSDTINLLAALGQIRSLLSVRMGKEEELLMINGLGDIMN 2050  
|||||  
2050 NKVFYQHHPNLMRVLGMHETVMEVMVNVLGTEKSQIAFPKMVASCCFELCY 2099  
|||||  
2051 NKVFYQHHPNLMRVLGMHETVMEVMVNVLGTEKSQIAFPKMVASCCFELCY 2100  
|||||  
2100 FCRISRQNKAMFEHLSYLLENSSVGLASPSMRGSTPLDVAASSVMDNNE 2149  
|||||  
2101 FCRISRQNKAMFEHLSYLLENSSVGLASPSMRGSTPLDVAASSVMDNNE 2150  
|||||  
2150 LALSLEEPDLEKVVVTYLAGCGLQSCPMLLAKGYPDVGWNPIEGERYLSFL 2199  
|||||  
2151 LALSLEEPDLEKVVVTYLAGCGLQSCPMLLAKGYPDVGWNPIEGERYLSFL 2200

FIG. 39 (CONT.<sup>8</sup>)

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2200 RFAVFNSESVENASVVVKLLIRRPECFCGPALRGEGNGLLAAMQGAIK 2249  
|||||  
2201 RFAVFNSESVENASVVVKLLIRRPECFCGPALRGEGNGLLAAMQGAIK 2250  
|||||  
2250 ISENPALDLP SQGYKREVSTEDDEEEEEIVHMGNAIMSFYSALIDLLGRC 2299  
|||||  
2251 ISENPALDLP SQGYKREVSTEDDEEEEEIVHMGNAIMSFYSALIDLLGRC 2300  
|||||  
2300 APEMHLIQTGKGEAIRIRSIILRSLVPTEDLVGIIISIPKLPSLNKDGVS 2349  
|||||  
2301 APEMHLIQTGKGEAIRIRSIILRSLVPTEDLVGIIISIPKLPSLNKDGVS 2350  
|||||  
2350 EPDMAXNFCPDHKA PMVLF LDRVYGIKDQTFLLHLLLEVGF L PDLRASASL 2399  
|||||  
2351 EPDMAGNFCPDHKA PMVLF LDRVYGIKDQTFLLHLLLEVGF L PDLRASASL 2400  
|||||  
2400 DTVSLSTTEAALALNRYICS AVLP LLTRCAPLFXGTEHCTSLIDSTLQTI 2449  
|||||  
2401 DTVSLSTTEAALALNRYICS AVLP LLTRCAPLFXGTEHCTSLIDSTLQTI 2450

FIG. 39 (CONT.)

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2450 YRLSKGRSLTKAQRDTIEECCLLAICNHLRPSMLQQLRRLVFDVPQLNEY 2499  
|||||  
2451 YRLSKGRSLTKAQRDTIEECCLLAICNHLRPSMLQQLRRLVFDVPQLNEY 2500  
.  
2500 CKMPLKLLTNHYEQCWKYCYCLPSGWGSYGLAVEEEHLHLTEKLFWGIXDLSL 2549  
|||||  
2501 CKMPLKLLTNHYEQCWKYCYCLPSGWGSYGLAVEEEHLHLTEKLFWGIIDSL 2550  
.  
2550 SHKKYDPPDLFRMALPCLSAIAGALPPDYLDXRITATLEKQISVDADGNFD 2599  
|||||  
2551 SHKKYDPPDLFRMALPCLSAIAGALPPDYLDXRITATLEKQISVDADGNFD 2600  
.  
2600 PKPINTMNFSLPEKLEYIVTKYAEHSHDKWACDKSQSGWKYGISLDENVK 2649  
|||||  
2601 PKPINTMNFSLPEKLEYIVTKYAEHSHDKWACDKSQSGWKYGISLDENVK 2650  
.  
2650 THPLIRPFKTLTEKEKEIYRWPARESLKTMLAVGWTVERTKEGEALVQQR 2699  
|||||  
2651 THPLIRPFKTLTEKEKEIYRWPARESLKTMLAVGWTVERTKEGEALVQQR 2700

FIG. 39 (CONT.<sup>10</sup>)

2700	ENEKLRVSQANQNSYSPAPLDLSNVVLSRELQGMVEVVAENYHNIWAK	2749
2701	ENEKLRVSQANQNSYSPAPLDLSNVVLSRELQGMVEVVAENYHNIWAK	2750
2750	KKKLELESKGGSHPLLVPYDTLTAAKEKFKDREKAQDLFKFLQVNGIIVS	2799
2751	KKKLELESKGGSHPLLVPYDTLTAAKEKFKDREKAQDLFKFLQVNGIIVS	2800
2800	RGMKDMELDASSMEKRFXYKFLKKILKYVDSAQEFIAHLEAIVSSGKTEK	2849
2801	RGMKDMELDASSMEKRFYKFLKKILKYVDSAQEFIAHLEAIVSSGKTEK	2850
2850	SPRDQEIKEFFAKVLLPLVDQYFTSHCLYFLSSPLKPLSSSGYASHKEKEM	2899
2851	SPRDQEIKEFFAKVLLPLVDQYFTSHCLYFLSSPLKPLSSSGYASHKEKEM	2900
2900	VAGLFCKLAALVRHRISLFGSDSTTMVSC LHILAQTLDTRTVMKSGSELV	2949
2901	VAGLFCKLAALVRHRISLFGSDSTTMVSC LHILAQTLDTRTVMKSGSELV	2950

FIG. 39 (CONT.<sup>11</sup>)



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2950 KAGLRAFFENAAEDLEKTS<sup>.</sup>ENLKL<sup>.</sup>GKFT<sup>.</sup>HSRTQIKGVSQNIN<sup>.</sup>YTTVALLP 2999  
|||||  
2951 KAGLRAFFENAAEDLEKTS<sup>.</sup>ENLKL<sup>.</sup>GKFT<sup>.</sup>HSRTQIKGVSQNIN<sup>.</sup>YTTVALLP 3000  
|||||  
3000 ILTSIFEHVTQH<sup>.</sup>QFGMDLL<sup>.</sup>LGDVQIS<sup>.</sup>CYHILCSLYSLGTGKNIY<sup>.</sup>VERQRP 3049  
|||||  
3001 ILTSIFEHVTQH<sup>.</sup>QFGMDLL<sup>.</sup>LGDVQIS<sup>.</sup>CYHILCSLYSLGTGKNIY<sup>.</sup>VERQRP 3050  
|||||  
3050 ALGECLASLAAAI<sup>.</sup>PVAFLEPTLNRYNPLSV<sup>.</sup>FN<sup>.</sup>TKTPRERSILGMPDT<sup>.</sup>VED 3099  
|||||  
3051 ALGECLASLAAAI<sup>.</sup>PVAFLEPTLNRYNPLSV<sup>.</sup>FN<sup>.</sup>TKTPRERSILGMPDT<sup>.</sup>VED 3100  
|||||  
3100 MCPDIPQLEGLMKEIND<sup>.</sup>LAESGARYTEM<sup>.</sup>PHVIEVILPMLCNYLSY<sup>.</sup>WWERG 3149  
|||||  
3101 MCPDIPQLEGLMKEIND<sup>.</sup>LAESGARYTEM<sup>.</sup>PHVIEVILPMLCNYLSY<sup>.</sup>WWERG 3150  
|||||  
3150 PENLPPSTG<sup>.</sup>PCCTKVTSEHLSLILGNILKIINN<sup>.</sup>NLGI<sup>.</sup>DEASW<sup>.</sup>MKRIA<sup>.</sup>VYA 3199  
|||||  
3151 PENLPPSTG<sup>.</sup>PCCTKVTSEHLSLILGNILKIINN<sup>.</sup>NLGI<sup>.</sup>DEASW<sup>.</sup>MKRIA<sup>.</sup>VYA 3200

FIG. 39 (CONT.<sup>12</sup>)



SUBSTITUTE SHEET (RULE 261)

FIG. 39 (CONT.<sup>14</sup>)

3700	EGLGMVTEEGTLIVRERGEKVLQNDFFTRDLFRFLQLLCEGHNSDFQNFL	3749
3701	EGLGMVTEEGTLIVRERGEKVLQNDFFTRDLFRFLQLLCEGHNSDFQNFL	3750
3750	RTQMGNTTTVNVIIISTVDYLLRLQESISDFYWYYSKGDIIDESGQHNFESK	3799
3751	RTQMGNTTTVNVIIISTVDYLLRLQESISDFYWYYSKGDIIDESGQHNFESK	3800
3800	ALAVTKQIFNSLTEYIQGPCIGNQQSLAHSRLWDVVGFLHVFANMQMKL	3849
3801	ALAVTKQIFNSLTEYIQGPCIGNQQSLAHSRLWDVVGFLHVFANMQMKL	3850
3850	SQDSSQIELLKELLDLQDMVVMLLSLLGNNVNGTIGKQMVDTLVESST	3899
3851	SQDSSQIELLKELLDLQDMVVMLLSLLGNNVNGTIGKQMVDTLVESST	3900
3900	NVEMILKFFDMFLKLDLTSSDTFKEYDPDGKGIISKKEFQKAMEGQKQY	3949
3901	NVEMILKFFDMFLKLDLTSSDTFKEYDPDGKGIISKKEFQKAMEGQKQY	3950

FIG. 39 (CONT.)<sup>15</sup>

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3950 TQSEIDFLLSCAEADENDMFNYVDFVDRFHEPAKDIGNVAVLLTNLSEH 3999  
|||||  
3951 TQSEIDFLLSCAEADENDMFNYVDFVDRFHEPAKDIGNVAVLLTNLSEH 4000  
|||||  
4000 MPNDSRLKCLDPAESVLNYFXPYLGRIEIMGAKKIERVYFEISESRT 4049  
|||||  
4001 MPNDSRLKCLDPAESVLNYFGPYLGRIEIMGAKKIERVYFEISESRT 4050  
|||||  
4050 QWEKPQVKESKRQFIFDVVNEGGEQKMXL FVNFCEDTIFEMQLASQISE 4099  
|||||  
4051 QWEKPQVKESKRQFIFDVVNEGGEQKMG L FVNFCEDTIFEMQLASQISE 4100  
|||||  
4100 SDSADRPEEEEEDEDDSSYVLEIAGEEEEEEDGSLEPASAFAMACASVKRNVT 4149  
|||||  
4101 SDSADRPEEEEEDEDDSSYVLEIAGEEEEEEDGSLEPASAFAMACASVKRNVT 4150  
|||||  
4150 DELKRATLKNLRKQYRNVKKMTAKELVKVLFSEFFWMLFVGLFQLLFTILG 4199  
|||||  
4151 DELKRATLKNLRKQYRNVKKMTAKELVKVLFSEFFWMLFVGLFQLLFTILG 4200

FIG. 39 (CONT.<sup>16</sup>)

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4200 GIFQILWSTVFGGGLVEGAKNIRVTKILGDMPTQFGIHDDTMEAEAE 4249  
|||||  
4201 GIFQILWSTVFGGGLVEGAKNIRVTKILGDMPTQFGIHDDTMEAEAE 4250  
|||||  
4250 VMEPGITTEL VHF I KGEKGD TDIMSDLFGLHPKKEGSLKHGPEVGLDLS 4299  
|||||  
4251 VMEPGITTEL VHF I KGEKGD TDIMSDLFGLHPKKEGSLKHGPEVGLDLS 4300  
|||||  
4300 EIIGKDEPPTLESTVQKKRKAQAAEMKAANEAEKGKVESEKADMEDGEKED 4349  
|||||  
4301 EIIGKDEPPTLESTVQKKRKAQAAEMKAANEAEKGKVESEKADMEDGEKED 4350  
|||||  
4350 KDKEEEQAEYLWTEVTKKKKRRRCQGQKVEKPEAFTANFFKGLEIYQTKLLH 4399  
|||||  
4351 KDKEEEQAEYLWTEVTKKKKRRRCQGQKVEKPEAFTANFFKGLEIYQTKLLH 4400  
|||||  
4400 YLARNFYNLRFALFVAFAINFILLFYKVTETEEPLEEETEDVANLWNSFND 4449  
|||||  
4401 YLARNFYNLRFALFVAFAINFILLFYKVTETEEPLEEETEDVANLWNSFND 4450

FIG. 39 (CONT.<sup>17</sup>)



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4700 PDMKCDDMMTCYLFHMYVGVRRAGGGIGDEIEDPAGDPYEMYRIVFDITFF 4749  
|||||  
4701 PDMKCDDMMTCYLFHMYVGVRRAGGGIGDEIEDPAGDPYEMYRIVFDITFF 4750  
|||||  
4750 FFVIVILLAI IQGLI IDAFGELRDQQEQVREDME 4783  
|||||  
4751 FFVIVILLAI IQGLI IDAFGELRDQQEQVREDME 4784

FIG. 39 (CONT.<sup>19</sup>)



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1 MRTLLPPALLTCWLLAPVNSIHPECRFHLEIQEEETKCXELLRSQTEKHK 50  
|||||  
1 MRTLLPPALLTCWLLAPVNSIHPECRFHLEIQEEETKCAELLRSQTEKHK 50

51 ACSGVWDNITCWRPANVGETVTPCPKVFNSFYKAGNISKNCTSDGWSE 100  
|||||  
51 ACSGVWDNITCWRPANVGETVTPCPKVFNSFYKAGNISKNCTSDGWSE 100

101 TFPDFVDACGYSDPEDESKITFYILVKAIYTLGYSVSLMSLATGSIILCL 150  
|||||  
101 TFPDFVDACGYSDPEDESKITFYILVKAIYTLGYSVSLMSLATGSIILCL 150

151 FRKLHCTRNYIHLNLFSLFILRAISVLVKDDVLYSSSGTLHCPDQPSWV 200  
|||||  
151 FRKLHCTRNYIHLNLFSLFILRAISVLVKDDVLYSSSGTLHCPDQPSWV 200

201 GCKLSLVFLQCYCIMANFFWLLVEGLYLHTLLVAMLPRRRCFLAYLLIGWG 250  
|||||  
201 GCKLSLVFLQCYCIMANFFWLLVEGLYLHTLLVAMLPRRRCFLAYLLIGWG 250

FIG. 40





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230 LFTLLVETFFPERRRYFYWYTIIGWGTPPTVCVTWATLRLYFDDTGCWDMN 279  
|||||  
251 LFTLLVETFFPERRRYFYWYTIIGWGTPPTVCVTWATLRLYFDDTGCWDMN 300  
|||||  
280 DSTALWWVIKGPVVGSIMVNFVLFIGIIVILVQKLQSPDMGGNESSIYLR 329  
|||||  
301 DSTALWWVIKGPVVGSIMVNFVLFIGIIVILVQKLQSPDMGGNESSIYLR 350  
|||||  
330 LARSTLLLIPLFGIHYTVFAFSPENVSKRERLVFELGLGSFQGFVVAVLY 379  
|||||  
351 LARSTLLLIPLFGIHYTVFAFSPENVSKRERLVFELGLGSFQGFVVAVLY 400  
|||||  
380 CFLNGEVQAEIKRKWRSWKVNRYFAVDEKHRHPSLASSGVNGGTQLSILS 429  
|||||  
401 CFLNGEVQAEIKRKWRSWKVNRYFAVDEKHRHPSLASSGVNGGTQLSILS 450  
|||||  
430 KSSSQIRMSGGLPADNLAT 447  
|||||  
451 KSSSQIRMSGGLPADNLAT 468

FIG. 41 (CONT.<sup>1</sup>)

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1 MERGLPLLCAVLALVAPAGAFNRDKCGDTIKIESPGYLTSPPGYPHSYHP 50  
|||||  
1 MERGLPLLCAVLALVAPAGAFNRDECGDTIKIESPGYLTSPPGYPHSYHP 50  
51 SEKCEWLIQAPDPYQRIMINFNFHFDLEDRDCKYDYVEVFDGENENGHER 100  
|||||  
51 SEKCEWLIQAPDPYQRIMINFNFHFDLEDRDCKYDYVEVFDGENENGHER 100  
101 GKFCGKIAPPPVSSGPFLLFIKFVSDYETHGAGFSIRYEIFKRGPECSQN 150  
|||||  
101 GKFCGKIAPPPVSSGPFLLFIKFVSDYETHGAGFSIRYEIFKRGPECSQN 150  
151 YTPSGVIKSPGFPEKYPNSLECTYIVFAPKMSEIILEFESFDLEPDSNP 200  
|||||  
151 YTPSGVIKSPGFPEKYPNSLECTYIVFAPKMSEIILEFESFDLEPDSNP 200  
201 PGGMFCRYDRLEIWDGFPDVGPVPHIGRYCGQKTPGRIRSSSGILSMVFYTD 250  
|||||  
201 PGGMFCRYDRLEIWDGFPDVGPVPHIGRYCGQKTPGRIRSSSGILSMVFYTD 250

FIG. 42

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```

251  SAIKEGFSANYSVLQSSVSEDFKCM EALGMESGEIHSDQITASSQYSTN 300
    |||||
251  SAIKEGFSANYSVLQSSVSEDFKCM EALGMESGEIHSDQITASSQYSTN 300
    |||||
301  WSAERSRLNYPENGWTPGEDSYREWIQVDLGLLRFVTA VGTQGAISKETK 350
    |||||
301  WSAERSRLNYPENGWTPGEDSYREWIQVDLGLLRFVTA VGTQGAISKETK 350
    |||||
    351  KKYYVVKTYKIDVSSNGEDWITIKEGNKPVV 380
        |||||
    351  KKYYVVKTYKIDVSSNGEDWITIKEGNK PVL 380

```

**FIG. 42 (CONT.<sup>1</sup>)**

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1 MERGLPLLCAVLALVAPAGAFRNDCEGDTIKIESPGYLTSPPGYPHSYHP 50  
51 SEKCEWLIQAPDPYQRIMINFNPHFDLED RDCKYDYVEFDGENENGHFR 100  
|||||  
51 SEKCEWLIQAPDPYQRIMINFNPHFDLED RDCKYDYVEFDGENENGHFR 100  
101 GKFCGKIAPPPVSSGPFLEIKFVSDYETHGAGFSIRYEIFKRGPECSQN 150  
|||||  
101 GKFCGKIAPPPVSSGPFLEIKFVSDYETHGAGFSIRYEIFKRGPECSQN 150  
151 YTPSGVIKSPGFPEKYPNSLECTYIVFAPKMSEIILEFESFDLEPDSNP 200  
|||||  
151 YTPSGVIKSPGFPEKYPNSLECTYIVFAPKMSEIILEFESFDLEPDSNP 200  
201 PGMFCRYDRLEIWDGFPDVGPHIGRYCGQKTPGRIRSSSGILSMVFYTD 250  
|||||  
201 PGMFCRYDRLEIWDGFPDVGPHIGRYCGQKTPGRIRSSSGILSMVFYTD 250

FIG. 43





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1 MGRVGYWTLLVLPALLVWRGPAPSAAAEKGPALNIAVMLGSHDVTRE 50  
|||||  
1 MGRVGYWTLLVLPALLVWRGPAPSAAAEKGPALNIAVMLGSHDVTRE 50

51 LRTLWGPEQAAGLPLDVNVVALLMNRTPKSLITHVCDLMSGARIHGLVF 100  
|||||  
51 LRTLWGPEQAAGLPLDVNVVALLMNRTPKSLITHVCDLMSGARIHGLVF 100

101 GDDTDQEAQAQMLDFISSHTFVPILGIHGGASMIMADKDPSTFFQFGAS 150  
|||||  
101 GDDTDQEAQAQMLDFISSHTFVPILGIHGGASMIMADKDPSTFFQFGAS 150

151 IQQQATVMLKIMQDYDWHVFSLVTTIFPGYREFISFVKTVDNSFVGWDM 200  
|||||  
151 IQQQATVMLKIMQDYDWHVFSLVTTIFPGYREFISFVKTVDNSFVGWDM 200

201 QNVITLDTSEDAKTQVQLKKIHSSVILLYCSKDEAVLILSEARSLGLTG 250  
|||||  
201 QNVITLDTSEDAKTQVQLKKIHSSVILLYCSKDEAVLILSEARSLGLTG 250

FIG. 44



501	VYQRAVMAVGLTINEERSEVVD	FSVPFVETGISVMVSR	NGTVSPSAFL	550	
501	VYQRAVMAVGLTINEERSEVVD	FSVPFVETGISVMVSR	NGTVSPSAFL	550	
551	EPFSASVWVMFVMLLIVSAIA	VEFVEYFSPVGYNRNLAKG	APHGPSET	600	
551	EPFSASVWVMFVMLLIVSAIA	VEFVEYFSPVGYNRNLAKG	APHGPSET	600	
601	IGKAIWLLWGLVFNN	SVPVQNPKGTTSKIMSV	WAFFAVIFLAS	650	
601	IGKAIWLLWGLVFNN	SVPVQNPKGTTSKIMSV	WAFFAVIFLAS	650	
651	AFMIQEEFVDQVTGLSDKK	FQRP	HDYSPPF	FGTVPNGSTERNIRNN	700
651	AFMIQEEFVDQVTGLSDKK	FQRP	HDYSPPF	FGTVPNGSTERNIRNN	700

**FIG. 44 (CONT.<sup>2</sup>)**

[illegible]

**FIG. 44 (CONT.<sup>3</sup>)**

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951 GKESIFGDNMNELQTFVANRQKDNLNYYVFQGGHPLTLNESNPNTVEVAV 1000  
|||||  
951 GKESIFGDNMNELQTFVANRQKDNLNYYVFQGGHPLTLNESNPNTVEVAV 1000  
1001 STESKANSRPRQLWKKSVD SIRQDSLSQNPVSQRDEATAENRTHSLKSPR 1050  
|||||  
1001 STESKANSRPRQLWKKSVD SIRQDSLSQNPVSQRDEATAENRTHSLKSPR 1050  
1051 YLPEEMAHSDISETSNRATCHREPDNSKNHKTKDNFKRSVASKYPKDCSE 1100  
|||||  
1051 YLPEEMAHSDISETSNRATCHREPDNSKNHKTKDNFKRSVASKYPKDCSE 1100  
1101 VERTYLKTKSSSPRDKIYTI DGEKEPGFHLDPQFVENVTLPENVDFFDP 1150  
|||||  
1101 VERTYLKTKSSSPRDKIYTI DGEKEPGFHLDPQFVENVTLPENVDFFDP 1150  
1151 YQDPSENF RKGDSTLPMNRNPLHNEEGLSNNDQYKLYSKHFTLKDKGSPH 1200  
|||||  
1151 YQDPSENF RKGDSTLPMNRNPLHNEEGLSNNDQYKLYSKHFTLKDKGSPH 1200

FIG. 44 (CONT. 4)



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1 MRTLLPPALLTCWLLAPVNSIHPECRFHLEIQEEETKCXELLRSQTEKHK 50  
|||||  
1 MRTLLPPALLTCWLLAPVNSIHPECRFHLEIQEEETKCAELLRSQTEKHK 50  
51 ACSGVWDNITCWRPANVGETVTVPCPKVFNSFYSKAGNISKNCTSDGWSE 100  
|||||  
51 ACSGVWDNITCWRPANVGETVTVPCPKVFNSFYSKAGNISKNCTSDGWSE 100  
101 TFPDFVDACGYSDPEDESKITFYILVKAIYTLGYSVSLMSLATGSIILCL 150  
|||||  
101 TFPDFVDACGYSDPEDESKITFYILVKAIYTLGYSVSLMSLATGSIILCL 150  
151 FRKLHCTRNYIHLNLFSLFILRAISVLVKDDVLYSSSGTLHCPDQPSSWV 200  
|||||  
151 FRKLHCTRNYIHLNLFSLFILRAISVLVKDDVLYSSSGTLHCPDQPSSWV 200  
201 GCKLSLVFLQYCIMANFFWLLVEGLYLHTLLVAMLPPRRRCFLAYLLIGWG 250  
|||||  
201 GCKLSLVFLQYCIMANFFWLLVEGLYLHTLLVAMLPPRRRCFLAYLLIGWG 250

FIG. 45

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251 LPTVCIGAWTAARLYLEDTCGWDNDHSDVPWWVIRIPILISIIVNFVLF 300  
|||||  
251 LPTVCIGAWTAARLYLEDTCGWDNDHSDVPWWVIRIPILISIIVNFVLF 300  
301 SIIRILLQKLTSPDVGGNDQSQYKRLAKSTLLLIPLFGVHYMVFAVEPIS 350  
|||||  
301 SIIRILLQKLTSPDVGGNDQSQYKRLAKSTLLLIPLFGVHYMVFAVEPIS 350  
351 ISSKYQILFELCLGSGFQGLVVAVLYCFLNSEV 382  
|||||  
351 ISSKYQILFELCLGSGFQGLVVAVLYCFLNSEV 382

FIG. 45 (CONT.<sup>1</sup>)



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1 MRTLLPPALLTCWLLAPVNSIHPECRFHLEIQEEETKCXELLRSQTEKHK 50  
|||||  
1 MRTLLPPALLTCWLLAPVNSIHPECRFHLEIQEEETKCAELLRSQTEKHK 50  
51 ACSGVWDNITCWRPANVGETVTPCPKVFSNFYSKAGNISKNCTSDGWSE 100  
|||||  
51 ACSGVWDNITCWRPANVGETVTPCPKVFSNFYSKAGNISKNCTSDGWSE 100  
101 TFPDFVDACGYSDPEDESKITFYILVKAIYTLGYSVSLMSLATGSIILCL 150  
|||||  
101 TFPDFVDACGYSDPEDESKITFYILVKAIYTLGYSVSLMSLATGSIILCL 150  
151 FRKLHCTRNYIHLNLFSLFILRAISVLVKDDVLYSSSGTLHCPDQPSSWV 200  
|||||  
151 FRKLHCTRNYIHLNLFSLFILRAISVLVKDDVLYSSSGTLHCPDQPSSWV 200  
201 GCKLSLVFLQCYCIMANFFWLLVEGLYLHTLLVAMPLPPRRCFLAYLLIGWG 250  
|||||  
201 GCKLSLVFLQCYCIMANFFWLLVEGLYLHTLLVAMPLPPRRCFLAYLLIGWG 250

FIG. 46

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251 LPTVCIGAWTAARLYLEDTCGWDTNDHSPVWVIRIPILISIIVNFVLEFI 300  
|||||  
251 LPTVCIGAWTAARLYLEDTCGWDTNDHSPVWVIRIPILISIIVNFVLEFI 300  
301 SIIRILLQKLTSPPDVGNDQSQYKRLAKSTLLLIPLFGVHYMVFAVFPIS 350  
|||||  
301 SIIRILLQKLTSPPDVGNDQSQYKRLAKSTLLLIPLFGVHYMVFAVFPIS 350  
351 ISSKYQILFELCLGSFQGLVVAVLYCFLNSEV 382  
|||||  
351 ISSKYQILFELCLGSFQGLVVAVLYCFLNSEV 382

FIG. 46 (CONT.<sup>1</sup>)

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1 MKSGSGGSPTSLWGLFLFLSAALSLWPTSGEICGPGIDIRNDYQQLKRL 50  
|||||  
1 MKSGSGGSPTSLWGLFLFLSAALSLWPTSGEICGPGIDIRNDYQQLKRL 50

51 NCTVIEGYLHILLISKAEDYRSYRFPKLTVITEYLLLFVAGLESLGDLF 100  
|||||  
51 NCTVIEGYLHILLISKAEDYRSYRFPKLTVITEYLLLFVAGLESLGDLF 100

101 PNLTVIRGWKLFYNYALVIFEMTNLKDIGLYNLRNITRGAIRIEKNADLC 150  
|||||  
101 PNLTVIRGWKLFYNYALVIFEMTNLKDIGLYNLRNITRGAIRIEKNADLC 150

151 YLSTVDWSLILDVSNYYIVGNKPPKECGDLCPGTMEEKPMCEKTTINNE 200  
|||||  
151 YLSTVDWSLILDVSNYYIVGNKPPKECGDLCPGTMEEKPMCEKTTINNE 200

201 YNYRCWTTNRCQKMCPSCTCGKRACTENNECHPECLGSCSAPDNDTACVA 250  
|||||  
201 YNYRCWTTNRCQKMCPSCTCGKRACTENNECHPECLGSCSAPDNDTACVA 250

FIG. 47

251	CRHYYAGVCPACPPNTYRFEGWRCVDRDFCANILSAESSDSEGFVIHD	300
251	CRHYYAGVCPACPPNTYRFEGWRCVDRDFCANILSAESSDSEGFVIHD	300
301	GECMQECPSGFIRNGSQSMYCIPEGPCPKVCEEEKTKTIDSVTSAQML	350
301	GECMQECPSGFIRNGSQSMYCIPEGPCPKVCEEEKTKTIDSVTSAQML	350
351	QGCTIFKGNLLINIRRGNNIASELENFMGLIEVVTGYVKIRHSHALVSLS	400
351	QGCTIFKGNLLINIRRGNNIASELENFMGLIEVVTGYVKIRHSHALVSLS	400
401	FLKNLRLILGEEQLEGNYSFYVLDNQNLQQLWDWDHRNLTIKAGKMYFAF	450
401	FLKNLRLILGEEQLEGNYSFYVLDNQNLQQLWDWDHRNLTIKAGKMYFAF	450
451	NPKLCVSEIYRMEEVGTGKGRQSKGDINTRNNGERASCESDVLHFTSTTT	500
451	NPKLCVSEIYRMEEVGTGKGRQSKGDINTRNNGERASCESDVLHFTSTTT	500

FIG. 47 (CONT.)<sup>1</sup>)

5501	SKNR	II	TW	HR	YR	PP	DY	RD	LIS	FT	VY	YK	EAP	FKN	VTE	YD	GQ	DAC	GNS	WN	550					
																				550						
5501	SKNR	II	TW	HR	YR	PP	DY	RD	LIS	FT	VY	YK	EAP	FKN	VTE	YD	GQ	DAC	GNS	WN	550					
551	MVDV	DL	PP	KN	DV	EP	GILL	HGL	KP	WT	QY	AV	YV	KAV	TL	TM	VEND	HIR	GA	KS	600					
																				600						
551	MVDV	DL	PP	KN	DV	EP	GILL	HGL	KP	WT	QY	AV	YV	KAV	TL	TM	VEND	HIR	GA	KS	600					
601	ILYI	RT	NA	SV	PS	IP	LD	VL	SA	SN	SS	QL	IV	KN	PP	SL	PN	GN	LS	YI	VR	WQ	650			
																				650						
601	ILYI	RT	NA	SV	PS	IP	LD	VL	SA	SN	SS	QL	IV	KN	PP	SL	PN	GN	LS	YI	VR	WQ	650			
651	QPQD	GY	LY	RH	NY	CS	KD	KI	PI	RK	YA	DG	TI	DI	EE	VT	EN	PK	TE	VC	GG	EK	GP	CC	700	
																								700		
651	QPQD	GY	LY	RH	NY	CS	KD	KI	PI	RK	YA	DG	TI	DI	EE	VT	EN	PK	TE	VC	GG	EK	GP	CC	700	
701	ACP	K	TE	AE	KQ	AE	KE	EE	AE	YR	KV	FE	NF	LH	NS	IF	VP	RP	ER	KR	RD	VM	QV	AN	TT	750
																									750	
701	ACP	K	TE	AE	KQ	AE	KE	EE	AE	YR	KV	FE	NF	LH	NS	IF	VP	RP	ER	KR	RD	VM	QV	AN	TT	750

**FIG. 47 (CONT.<sup>2</sup>)**



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```

1001 MSRELGGQSGFMVYEGVAKGVVKDEPETRVAIKTVNEAASMRERIEFLNE 1050
|||||
1001 MSRELGGQSGFMVYEGVAKGVVKDEPETRVAIKTVNEAASMRERIEFLNE 1050

1051 ASVMKEFNCHHVRLGLGVVSQGQPTLVIMELMTRGDLKSYLSLRPEMEN 1100
|||||
1051 ASVMKEFNCHHVRLGLGVVSQGQPTLVIMELMTRGDLKSYLSLRPEMEN 1100

1101 NPVLAPPSLSKMIQAGEIADGMAYLNANKFVHRDLAARNCMVAEDFTVK 1150
|||||
1101 NPVLAPPSLSKMIQAGEIADGMAYLNANKFVHRDLAARNCMVAEDFTVK 1150

1151 IGDFGMTRDIYETDYRKGGKGLLPVRWMSPELKDGVFTTYSVDVWSFGV 1200
|||||
1151 IGDFGMTRDIYETDYRKGGKGLLPVRWMSPELKDGVFTTYSVDVWSFGV 1200

1201 VLWEIATLAEQPYQGLSNEQVLRVFMEGGLLDKPDNCPDMLFELMRMCWQ 1250
|||||
1201 VLWEIATLAEQPYQGLSNEQVLRVFMEGGLLDKPDNCPDMLFELMRMCWQ 1250

```

FIG. 47 (CONT.<sup>4</sup>)

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1251 YNP<sup>.</sup>KMR<sup>.</sup>PSFLEIISSIK.....EELDLEPENM 1277  
|||||  
1251 YNP<sup>.</sup>KMR<sup>.</sup>PSFLEIISSIK<sup>.</sup>EE<sup>.</sup>MPGFREV<sup>.</sup>SFY<sup>.</sup>SEENK<sup>.</sup>LP<sup>.</sup>EE<sup>.</sup>LDLEPENM 1300  
|||||  
1278 E<sup>.</sup>SVPLD<sup>.</sup>PSASS<sup>.</sup>SLPL<sup>.</sup>DRH<sup>.</sup>SGHKA<sup>.</sup>ENG<sup>.</sup>PG<sup>.</sup>VL<sup>.</sup>VRAS<sup>.</sup>FD<sup>.</sup>ERQ<sup>.</sup>PYA<sup>.</sup>HMN 1327  
|||||  
1301 E<sup>.</sup>SVPLD<sup>.</sup>PSASS<sup>.</sup>SLPL<sup>.</sup>DRH<sup>.</sup>SGHKA<sup>.</sup>ENG<sup>.</sup>PG<sup>.</sup>VL<sup>.</sup>VRAS<sup>.</sup>FD<sup>.</sup>ERQ<sup>.</sup>PYA<sup>.</sup>HMN 1350  
|||||  
1328 GGRKNERALPLPQSS<sup>.</sup>TC 1344  
|||||  
1351 GGRKNERALPLPQSS<sup>.</sup>TC 1367

FIG. 47 (CONT.<sup>5</sup>)





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251 SAIKEGFSANYSVLQSSVSEDFKMEALGMESGEIHSDQITASSQYSTN 300  
|||||  
251 SAIKEGFSANYSVLQSSVSEDFKMEALGMESGEIHSDQITASSQYSTN 300  
301 WSAERSRLNYPENGWTPGSDSYREWIQVDLGLLRFVTAVGTQGAISKETK 350  
|||||  
301 WSAERSRLNYPENGWTPGSDSYREWIQVDLGLLRFVTAVGTQGAISKETK 350  
351 KKYVVKTYKIDVSSNGEDWITIKEGNKPVLFQGNTPD VVAVFPKPLI 400  
|||||  
351 KKYVVKTYKIDVSSNGEDWITIKEGNKPVLFQGNTPD VVAVFPKPLI 400  
401 TRFVRIKPATWETGISMRFEVYGCKITDYPCSGMLGMVSLISDSQITSS 450  
|||||  
401 TRFVRIKPATWETGISMRFEVYGCKITDYPCSGMLGMVSLISDSQITSS 450  
451 NQGDRNWMPENIRLVTSRSGWALPPAPHSYINEWLQIDLGEKIVRGII 500  
|||||  
451 NQGDRNWMPENIRLVTSRSGWALPPAPHSYINEWLQIDLGEKIVRGII 500

FIG. 48 (CONT.<sup>1</sup>)

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501 QGKHKRENKVFMRKFKIGYSNNGSDWKIMDDSKRKAKSFEGNNNYDTPE 550  
|||||  
501 QGKHKRENKVFMRKFKIGYSNNGSDWKIMDDSKRKAKSFEGNNNYDTPE 550  
551 LRTFPALSTRFIRIYPERATHGGGLGRMELLGCEVEAPTAGPTTPNGNLV 600  
|||||  
551 LRTFPALSTRFIRIYPERATHGGGLGRMELLGCEVEAPTAGPTTPNGNLV 600  
601 DECDDDDQANCHSGTGDDFQLTGGTTVLATEKPTVIDSTIQS 641  
|||||  
601 DECDDDDQANCHSGTGDDFQLTGGTTVLATEKPTVIDSTIQS 641

FIG. 48 (CONT.<sup>2</sup>)

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1 MERGLPLLCAVLALVAPAGAFRNDKCGDTIKIESPGYLTSYGPHSYHP 50  
|||||  
1 MERGLPLLCAVLALVAPAGAFRNDKCGDTIKIESPGYLTSYGPHSYHP 50

51 SEKCEWLIQAPDPYQIRIMINFNPHFDLED RDCKYDYVEVFDGENENGHFR 100  
|||||  
51 SEKCEWLIQAPDPYQIRIMINFNPHFDLED RDCKYDYVEVFDGENENGHFR 100

101 GKFCGKIAPPPVSSGPFLLFIKFVSDYETHGAGFSIRYEIFKRGPECSQN 150  
|||||  
101 GKFCGKIAPPPVSSGPFLLFIKFVSDYETHGAGFSIRYEIFKRGPECSQN 150

151 YTPSGVIKSPGFPEKYPNSLECTYIVFAPKMSEIILEFESFDLEPDSNP 200  
|||||  
151 YTPSGVIKSPGFPEKYPNSLECTYIVFAPKMSEIILEFESFDLEPDSNP 200

201 PGGMFCRYDRLEIWDGFDPVGP HIGRYCGQKTPGRIRSSSGILSMVFYTD 250  
|||||  
201 PGGMFCRYDRLEIWDGFDPVGP HIGRYCGQKTPGRIRSSSGILSMVFYTD 250

FIG. 49

251	SAIAKEGFSANYSVLQSSVSEDFKCMALGMESGEIHSDQITASSQYSTN	300
251	SAIAKEGFSANYSVLQSSVSEDFKCMALGMESGEIHSDQITASSQYSTN	300
301	WSAERSRLNYPENGWTPGEDSYREWIQVDLGLLRFTAVGTQGAISKETK	350
301	WSAERSRLNYPENGWTPGEDSYREWIQVDLGLLRFTAVGTQGAISKETK	350
351	KKYYVVKTYKIDVSSNGEDWITIKEGNKPVLFGQNTNPTDVVAVFPKPLI	400
351	KKYYVVKTYKIDVSSNGEDWITIKEGNKPVLFGQNTNPTDVVAVFPKPLI	400
401	TRFVRIKPATWETGISMRFEVYGCKITDYPCSGMLGMVSGLISDSQITSS	450
401	TRFVRIKPATWETGISMRFEVYGCKITDYPCSGMLGMVSGLISDSQITSS	450
451	NQGRNWMMPENIRLVTSRSGWALPPAPHSYINEWLQIDLGEKIVRGII	500
451	NQGRNWMMPENIRLVTSRSGWALPPAPHSYINEWLQIDLGEKIVRGII	500

**FIG. 49 (CONT.)<sup>1</sup>**

```

501 QGKHRENKVFMRKFKIGYSNNGSDWKIMDDSKRKAK..... 538
    | | | | | | | | | | | | | | | | | | | | | | | |
501 QGKHRENKVFMRKFKIGYSNNGSDWKIMDDSKRKAKSFE GNNNYDTPE 550
    .
    .
    .
539 .....GGTTVLATEKPTVIDSTIQSEFFPTYGFNC 567
    ' | | | | | | | | | | | | | | | | | | | | | | | |
601 DECDDQANCHSGTGDDFQLTGGTTVLATEKPTVIDSTIQSEFFPTYGFNC 650
    . . . . .
568 EFGWGSHKTFCHWEHDNHVQLKWSVLT SKTGPIQDHTGDGNFIYSQADEN 617
    | | | | | | | | | | | | | | | | | | | | | | | |
651 EFGWGSHKTFCHWEHDNHVQLKWSVLT SKTGPIQDHTGDGNFIYSQADEN 700
    . . . . .
618 QKGKVARLVSPVVYSQNSAHCMTFWYHMSGSHVGT LRVKLR YQKP E EYDQ 667
    | | | | | | | | | | | | | | | | | | | | | | | |
701 QKGKVARLVSPVVYSQNSAHCMTFWYHMSGSHVGT LRVKLR YQKP E EYDQ 750

```

**FIG. 49 (CONT. <sup>2</sup>)**

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668 LVWMAIGHQGDHWKEGRVLLHKSLKLYQVIFEGEIGKGNLGGIAVDDISI 717  
|||||  
751 LVWMAIGHQGDHWKEGRVLLHKSLKLYQVIFEGEIGKGNLGGIAVDDISI 800  
718 NNHISQEDCAKPADLDKKNPEIKIDETGSTPGYEGEGEDKNISRKPGENV 767  
|||||  
801 NNHISQEDCAKPADLDKKNPEIKIDETGSTPGYEGEGEDKNISRKPGENV 850  
768 LKTLXPILITIIAMSALGVLLGAVCGVVLYCACWHNGMSENLNLSALENYN 817  
|||||  
851 LKTLXPILITIIAMSALGVLLGAVCGVVLYCACWHNGMSENLNLSALENYN 900  
818 FELVDGVKLLKKDKLNTQSTYSEA 840  
|||||  
901 FELVDGVKLLKKDKLNTQSTYSEA 923

FIG. 49 (CONT.<sup>3</sup>)





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301 WSAERSRLNYPENGWTPGEDSYREWIQVDLGLLRFTAVGTQGAISKETK 350  
|||||  
301 WSAERSRLNYPENGWTPGEDSYREWIQVDLGLLRFTAVGTQGAISKETK 350  
351 KKYVVKTYKIDVSSNGEDWITIKEGNKPVLFGQNTNPTDVVAVFPKPLI 400  
|||||  
351 KKYVVKTYKIDVSSNGEDWITIKEGNKPVLFGQNTNPTDVVAVFPKPLI 400  
401 TRFVRIKPATWETGISMRFEVYGCKITDYPCSGMLGMVSLISDSQITSS 450  
|||||  
401 TRFVRIKPATWETGISMRFEVYGCKITDYPCSGMLGMVSLISDSQITSS 450  
451 NQGDRNWMPENIRLVTSRSGWALPPAPHSYINNEWLQIDLGEKIVRGII 500  
|||||  
451 NQGDRNWMPENIRLVTSRSGWALPPAPHSYINNEWLQIDLGEKIVRGII 500  
501 QGGKHRENKVFMRKFKIGYSNNGSDWKIMDDSKRKAR 538  
|||||  
501 QGGKHRENKVFMRKFKIGYSNNGSDWKIMDDSKRKAK 538

FIG. 50 (CONT.<sup>1</sup>)

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1 MGAPACALALCVAVAI VAGASSESLGTEQRVVGRAAEVPGPEGGQEQLV 50  
|||||  
1 MGAPACALALCVAVAI VAGASSESLGTEQRVVGRAAEVPGPEGGQEQLV 50  
51 FGSGDAVELSCPPPGGGPMGPTVWVKDGTGLVPSE RVLVGPQRLQVLNAS 100  
|||||  
51 FGSGDAVELSCPPPGGGPMGPTVWVKDGTGLVPSE RVLVGPQRLQVLNAS 100  
101 HEDSGAYSCRQRLTQRVLCHF SVRVTDAPSSGDDDEGDEAEDTGVD TGA 150  
|||||  
101 HEDSGAYSCRQRLTQRVLCHF SVRVTDAPSSGDDDEGDEAEDTGVD TGA 150  
151 PYWTRPERMDKLLAVPAANTVRFRCPAAGNPTPSISWLKNGREFRGEHR 200  
|||||  
151 PYWTRPERMDKLLAVPAANTVRFRCPAAGNPTPSISWLKNGREFRGEHR 200  
201 IGGIKLRHQWLSLVMESVVPSPDRGN YTCVVENKFGSIRQTYTLDVLE RSP 250  
|||||  
201 IGGIKLRHQWLSLVMESVVPSPDRGN YTCVVENKFGSIRQTYTLDVLE RSP 250

FIG. 51

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251 HRPILQAGLPANQTAVLGSDVEFHCKVYSDAQPHIQWLKHVEVNGSKVGP 300  
|||||  
251 HRPILQAGLPANQTAVLGSDVEFHCKVYSDAQPHIQWLKHVEVNGSKVGP 300  
301 DGTPYVTVLKSWISESVEADVR.LRLANVSERDGGGEYLCRATNFIGVAEK 349  
|||||  
301 DGTPYVTVLKTAGANTTDKELEVLSLHNVTFFEDAGEYTCLAGNSIGFSHH 350  
350 AFWLSV 355  
351 SAWLVV 356

FIG. 51 (CONT.<sup>1</sup>)

```

1 MTLRHLPFILLILSGELYAEKQCDPFTVENGRIAQYYTTFKSFYFPMS 50
  |||||
1 MTLRHLPFILLILSGELYAEKQCDPFTVENGRIAQYYTTFKSFYFPMS 50

51 VDKKLSFFCLAGYATESGKQEEQIRCTAEGWSPNPRCYKKCLKPDLRNGY 100
  |||||
51 VDKKLSFFCLAGYATESGKQEEQIRCTAEGWSPNPRCYKKCLKPDLRNGY 100

101 VSNDKVLVKLQERMSYGCSSGYKTTGGKDEEVHCLSAGWSSQPSCRKEQ 150
  |||||
101 VSNDKVLVKLQERMSYGCSSGYKTTGGKDEEVHCLSAGWSSQPSCRKEQ 150

151 ETCLAPELEHGNYSTTQRTFKVKDIVAYTCTAGYTTTGKQTGEAECQAN 200
  |||||
151 ETCLAPELEHGNYSTTQRTFKVKDIVAYTCTAGYTTTGKQTGEAECQAN 200

201 GWSLTPQC�KLMCSSLRLIENGYFHPVKQTYEEGDVVQFFCHENYYLSGS 250
  |||||
201 GWSLTPQC�KLMCSSLRLIENGYFHPVKQTYEEGDVLVQFFCHENYYLSGS 250

```

**FIG. 52**

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251 DLIQCYNFGWYPESPICEGRRNRCPPPPVPLNSKIQPHSTTYRHGERVHI 300  
|||||  
251 DLIQCYNFGWYPESPICEGRRNRCPPPPVPLNSKIQPHSTTYRHGERVHI 300  
301 ECELNFVIQGSSEELLCENGKWTPEPKCI 328  
|||||  
301 ECELNFVIQGSSEELLCENGKWTPEPKCI 328

FIG. 52 (CONT.<sup>1</sup>)

```

1 MPWGRRPTWLLAFLLVFLKISILSVTAWQTGNCQPGPLERSERSGTCAG 50
  |||||
1 MPWGRRPTWLLAFLLVFLKISILSVTAWQTGNCQPGPLERSERSGTCAG 50

51 PAPFLVFSQKKSIRIDPDGTGNHQQLVVDAGISADMDIHYKKERLYWVDV 100
  |||||
51 PAPFLVFSQKKSIRIDPDGTGNHQQLVVDAGISADMDIHYKKERLYWVDV 100

101 ERQVLLRVFLNGTGLEKVCNVERKVSGLAIDWIDDEVLWVDQQNGVITVT 150
  |||||
101 ERQVLLRVFLNGTGLEKVCNVERKVSGLAIDWIDDEVLWVDQQNGVITVT 150

151 DMTGKNSRVLLSSLKHPNSIAVDPIERLMFWSSEVTGSLHRAHLKGVDVK 200
  |||||
151 DMTGKNSRVLLSSLKHPNSIAVDPIERLMFWSSEVTGSLHRAHLKGVDVK 200

201 TLLETGGISVLTLDVLDKRLFWVQDSGEGSHAYIHSCDYEAGSVRLIRHQ 250
  |||||
201 TLLETGGISVLTLDVLDKRLFWVQDSGEGSHAYIHSCDYEAGSVRLIRHQ 250

251 ARHSLSSMAFFGDRIFYSVLKSKAIWIANKHTGKDTVRLNHLPSFVTPGK 300
  |||||
251 ARHSLSSMAFFGDRIFYSVLKSKAIWIANKHTGKDTVRLNHLPSFVTPGK 300

```

**FIG. 53**

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301 LMVVHPRAQPRTEAAKDPPELLKQGRGPCRFGLCERDPKSHSSACAEG 350  
|||||  
301 LMVVHPRAQPRTEAAKDPPELLKQGRGPCRFGLCERDPKSHSSACAEG 350  
|||||  
351 YTLRDRKYCEDVNECATQNHGCTLGCENTPGSYHCTCPTGFVLLPDGKQ 400  
|||||  
351 YTLRDRKYCEDVNECATQNHGCTLGCENTPGSYHCTCPTGFVLLPDGKQ 400  
|||||  
401 CHELVSCPNGVSKCSHGCVLTSDGPRCICPAGSVLGRDGKTCTGCSSPDN 450  
|||||  
401 CHELVSCPNGVSKCSHGCVLTSDGPRCICPAGSVLGRDGKTCTGCSSPDN 450  
|||||  
451 GGCSQICLPLRPGSWECD CFPGYDLQSDRKSCAASGPQLLLFANSQDIR 500  
|||||  
451 GGCSQICLPLRPGSWECD CFPGYDLQSDRKSCAASGPQLLLFANSQDIR 500  
|||||  
501 HMFHDGTDYKVLLSRQMGVMFALDYDPVESKIYFAQTALKWIERANMDGS 550  
|||||  
501 HMFHDGTDYKVLLSRQMGVMFALDYDPVESKIYFAQTALKWIERANMDGS 550  
|||||  
551 QRLITEGVDTLEGLALDWIGRRIYWTDSGKSVVGGSDLGKHHRIIQ 600  
|||||  
551 QRLITEGVDTLEGLALDWIGRRIYWTDSGKSVVGGSDLGKHHRIIQ 600

FIG. 53 (CONT. <sup>1</sup>)

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601 ERISRPRGIAVHPRARRLFWTDVGMSPRIESASLQGS DRVLIASSNLLLEP 650  
|||||  
601 ERISRPRGIAVHPRARRLFWTDVGMSPRIESASLQGS DRVLIASSNLLLEP 650  
651 SGITIDYLTDTLYWCDTKRSVIE MANLDGSKRRRLIQNDVGH PFS LAVFE 700  
|||||  
651 SGITIDYLTDTLYWCDTKRSVIE MANLDGSKRRRLIQNDVGH PFS LAVFE 700  
701 DHLWVSDWAIPSVIRVNKRTGQNRVRLQGSMLKPSSLVVVHPLAKPGADP 750  
|||||  
701 DHLWVSDWAIPSVIRVNKRTGQNRVRLQGSMLKPSSLVVVHPLAKPGADP 750  
751 CLYRNGGCEHICQESLGTARCLCREGFVKAWDGKMC L PQDYPILSGENAD 800  
|||||  
751 CLYRNGGCEHICQESLGTARCLCREGFVKAWDGKMC L PQDYPILSGENAD 800  
801 LSKEVTSLSNSTQAEVPDDDGTESS TLVAEIMVSGMNYEDDCGPGCGGSH 850  
|||||  
801 LSKEVTSLSNSTQAEVPDDDGTESS TLVAEIMVSGMNYEDDCGPGCGGSH 850  
851 ARCVSDGETAECQCLKGFARDGNLCSDIDECVLARSDCPSTSSRCINTEG 900  
|||||  
851 ARCVSDGETAECQCLKGFARDGNLCSDIDECVLARSDCPSTSSRCINTEG 900

FIG. 53 (CONT.<sup>2</sup>)



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```

851  ARCVSDGETAECQCLKGFA RDGNLCSDIDECVLARSDCPSTSSRCINTEG 900
      |||||
851  ARCVSDGETAECQCLKGFA RDGNLCSDIDECVLARSDCPSTSSRCINTEG 900

901  GYVCRCEGYEGDGI SCFDIDECQ RGAHNCAENAACTNTEGGYNCTCAGR 950
      |||||
901  GYVCRCEGYEGDGI SCFDIDECQ RGAHNCAENAACTNTEGGYNCTCAGR 950

951  PSSPGLSCPDSTAPSL LGEDGHHLDRNSYPGCPSSYDGYCLNGGVCMHIE 1000
      |||||
951  PSSPGRSCPDSTAPSL LGEDGHHLDRNSYPGCPSSYDGYCLNGGVCMHIE 1000

1001 SLDSYTCNCVIGYSGDR CQT..... 1020
      |||||
1001 SLDSYTCNCVIGYSGDR CQTRDLRWELRHAGYGQKHDIMVVAVCMVALV 1050

1021 ..... PPSSDRGPQEIEGNSHLPSYRPVGPEKLHSLQSANG 1056
      |||||
1151 PHIDGMGTGQSCWIPPSSDRGPQEIEGNSHLPSYRPVGPEKLHSLQSANG 1200

      1057 SCHERAPDLPRQTEPVQ 1073
          |||||
      1201 SCHERAPDLPRQTEPVK 1217

```

Fig. 53 (Cont.)<sup>3</sup>

[illegible]

**FIG. 54**

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251 ARHSLSSMAFFGDRIFYVLKSKAIWANKHTGKDTVRLNHPSEFVTPGK 300  
|||||  
251 ARHSLSSMAFFGDRIFYVLKSKAIWANKHTGKDTVRLNHPSEFVTPGK 300  
|||||  
301 LMVVHPRAQPRTEAAKDPDPPELLKQGRGPCRFGLCERDPKSHSSACAEG 350  
|||||  
301 LMVVHPRAQPRTEAAKDPDPPELLKQGRGPCRFGLCERDPKSHSSACAEG 350  
|||||  
351 YTLSRDRKYCEDVNECATQNHGCTLGCENTPGSYHCTCPTGFVLLPDGKQ 400  
|||||  
351 YTLSRDRKYCEDVNECATQNHGCTLGCENTPGSYHCTCPTGFVLLPDGKQ 400  
|||||  
401 CHELVSCPGNVSKCSHGCVLTSDGPRCICPAGSVLGRDGKCTCGCSSPDN 450  
|||||  
401 CHELVSCPGNVSKCSHGCVLTSDGPRCICPAGSVLGRDGKCTCGCSSPDN 450  
|||||  
451 GGCSQICLPLRPGSWECDCEPGYDLQSDRKSCAASGPQPLL FANSQDIR 500  
|||||  
451 GGCSQICLPLRPGSWECDCEPGYDLQSDRKSCAASGPQPLL FANSQDIR 500  
|||||

FIG. 54 (CONT. <sup>1</sup>)

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501 HMFHFDGTDYKVLRSRQMGVMFALDYPDVESKIYFAQTALKWIERANMDGS 550  
|||||  
501 HMFHFDGTDYKVLRSRQMGVMFALDYPDVESKIYFAQTALKWIERANMDGS 550  
551 QRLITEGVDTLEGLALDWIGRRRIYWTDSGKSVVGGSDLGKHHRIIIQ 600  
|||||  
551 QRLITEGVDTLEGLALDWIGRRRIYWTDSGKSVVGGSDLGKHHRIIIQ 600  
601 ERISRPRGIAVHPRARRLFWTDVGMSPRIESASLQGS DRVLIASSNLLPEP 650  
|||||  
601 ERISRPRGIAVHPRARRLFWTDVGMSPRIESASLQGS DRVLIASSNLLPEP 650  
651 SGITIDYLTDTLYWC DTKRSVIE MANLDGSKRRRLIQNDVGH PFS LAVFE 700  
|||||  
651 SGITIDYLTDTLYWC DTKRSVIE MANLDGSKRRRLIQNDVGH PFS LAVFE 700  
701 DHLWVSDWAI PSVIRVNKRTGQNRVR LQGSMLK PSSLVVVHPLAKPGADP 750  
|||||  
701 DHLWVSDWAI PSVIRVNKRTGQNRVR LQGSMLK PSSLVVVHPLAKPGADP 750  
751 CLYRNGGCEHICQESLGTARCLCREGFVKAWDGKMC L P QDYPILSGENA 799  
|||||  
751 CLYRNGGCEHICQESLGTARCLCREGFVKAWDGKMC L P QDYPILSGENA 799

FIG. 54 (CONT. <sup>2</sup>)

```

1 MPWGRPTWLLAFLLVFLKISILSVTAWQTGNCQPGPLERSERSGTCAG 50
  |||||
1 MPWGRPTWLLAFLLVFLKISILSVTAWQTGNCQPGPLERSERSGTCAG 50
  . . . . . 66
51 PAPFLVFSQGKSISRI..... 66
  |||||
51 PAPFLVFSQGKSISRIDPDGTGNHQQLVVDAGISADMDIHYKKERLYWVDV 100
  .
67 .....WAIPSVIRVNKRTGQNRVRLQGSMCLKPSSLVVVHPLAKPGADP 109
  |||||
701DHLWVSDWAIPSVIRVNKRTGQNRVRLQGSMCLKPSSLVVVHPLAKPGADP 750
  .
110 CLYRNGGCEHICQESLGTARCLCREGFVKAWDGKMCCLPDYPILSGENAD 159
  |||||
751 CLYRNGGCEHICQESLGTARCLCREGFVKAWDGKMCCLPDYPILSGENAD 800
  .
160 LSKEVTSLSNSTQAEVPPDDGTESSTLVAEIMVSGMNYEDDCGPGCGSH 209
  |||||
801 LSKEVTSLSNSTQAEVPPDDGTESSTLVAEIMVSGMNYEDDCGPGCGSH 850

```

**FIG. 55**

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210 ARCVSDGETAECQCLKG FARDGNLCS DIDE CVLARSDCPSTSSRCINTEG 259  
|||||  
851 ARCVSDGETAECQCLKG FARDGNLCS DIDE CVLARSDCPSTSSRCINTEG 900  
|||||  
260 GYVCRCEGYEGDGI SCFDIDE CQRG AHNCAENAACTNTEGGYNCTCAGR 309  
|||||  
901 GYVCRCEGYEGDGI SCFDIDE CQRG AHNCAENAACTNTEGGYNCTCAGR 950  
|||||  
310 PSSPGLSCPDSTAPSL LGEDGHHLDRNSYPGCPSSYDGYCLNGGVCMHIE 359  
|||||  
951 PSSPGRSCPDSTAPSL LGEDGHHLDRNSYPGCPSSYDGYCLNGGVCMHIE 1000  
|||||  
360 SLDSYTCNCVIGYSGDR CQTRDLRWELRHAGYGQKHDIMVVAVCMVALV 409  
|||||  
1001 SLDSYTCNCVIGYSGDR CQTRDLRWELRHAGYGQKHDIMVVAVCMVALV 1050  
|||||  
410 LLLLLGMWGTYYYRTRKQLSNPPKNPCDEPSGSVSSSGPDSSSGAAVASC 459  
|||||  
1051 LLLLLGMWGTYYYRTRKQLSNPPKNPCDEPSGSVSSSGPDSSSGAAVASC 1100  
|||||

FIG. 55 (CONT. <sup>1</sup>)

460 PQPWFVLEKHQDPKNGSLPADGTNGAVVDAGLSPSLQLGSHLTSWRQK 509  
 11101 PQPWFVLEKHQDPKNGSLPADGTNGAVVDAGLSPSLQLGSHLTSWRQK 1150  
 510 PHIDGMGTGQSCWIPSSDRGPQIEGNSHLPSYRPVGPEKLHSLQSANG 559  
 11151 PHIDGMGTGQSCWIPSSDRGPQIEGNSHLPSYRPVGPEKLHSLQSANG 1200  
 560 SCHERAPDLPRQTEPVQ 576  
 1201 SCHERAPDLPRQTEPVK 1217

**FIG. 55 (CONT. <sup>2</sup>)**





```

210 LLLLGMWGTYYYRTRKQLSNPPKNPCDEPSGVSSSGPDSSSGAAVASC 259
    |||||
1051 LLLLGMWGTYYYRTRKQLSNPPKNPCDEPSGVSSSGPDSSSGAAVASC 1100
    |||||

260 PQPWFVLEKHQDPKNGSLPADGTNGAVVDAGLSPSLQLGSHLTSWRQK 309
    |||||
1101 PQPWFVLEKHQDPKNGSLPADGTNGAVVDAGLSPSLQLGSHLTSWRQK 1150
    |||||

310 PHIDGMGTQSCWIPPSSDRGPQIEGNSHLPSYRVPVGPEKLHSLQSANG 359
    |||||
1151 PHIDGMGTQSCWIPPSSDRGPQIEGNSHLPSYRVPVGPEKLHSLQSANG 1200
    |||||

360 SCHERAPDLPRQTEPVQ 376
    |||||
1201 SCHERAPDLPRQTEPVK 1217

```

**FIG. 56 (CONT.<sup>1</sup>)**

```

1 MGAASGQGRWPLSPPLMLSLVLLQSPAPALDPGLQPGNFSPDEAG 50
  |||||
1 MGAASGQGRWPLSPPLMLSLVLLQSPAPALDPGLQPGNFSPDEAG 50

51 AQLFAESYNSSAEVVMFQSTVASWAHDTNITEENARRQEEAALVSQEF 100
  |||||
51 AQLFAESYNSSAEVVMFQSTVASWAHDTNITEENARRQEEAALVSQEF 100

101 VWGKKAKELYESIWQNFTDSKLRRIIGSIRTLGPANLPLAQRQQYNSLLS 150
  |||||
101 VWGKKAKELYESIWQNFTDSKLRRIIGSIRTLGPANLPLAQRQQYNSLLS 150

151 NMSRIYSTGKVCFFPNKTATCWSLDPELTNILASSRSYAKLLFAWEGWHDA 200
  |||||
151 NMSRIYSTGKVCFFPNKTATCWSLDPELTNILASSRSYAKLLFAWEGWHDA 200

201 VGIPLKPLYQDFTAISNEAYRQDDFSDTGAFWRSWYESPSFEESLEHIYH 250
  |||||
201 VGIPLKPLYQDFTAISNEAYRQDDFSDTGAFWRSWYESPSFEESLEHIYH 250

```

**FIG. 57**

251	QLEPLYNLHAYVRRALHRRYGDKYVNLRGPIPAHLLGDMWAQSWENIYD	300
251	QLEPLYNLHAYVRRALHRRYGDKYVNLRGPIPAHLLGDMWAQSWENIYD	300
301	MVVPFPDKPNLDVTSTMVQKGNATHMFRVSEEFFTSGLSPMPPEFWAE	350
301	MVVPFPDKPNLDVTSTMVQKGNATHMFRVSEEFFTSGLSPMPPEFWAE	350
351	SMLEKPTDGREVVCHASAWDFYNRKDFRIKQCTRVTMEOQLATVHHMGHV	400
351	SMLEKPTDGREVVCHASAWDFYNRKDFRIKQCTRVTMEOQLATVHHMGHV	400
401	QYYLQYKDLHVSRLRGANPGFHEAIGDVLALSVPAPHLHKIGLLDHVTN	450
401	QYYLQYKDLHVSRLRGANPGFHEAIGDVLALSVPAPHLHKIGLLDHVTN	450
451	DIESDINYLKMALEKIAFLPFGYLVDQWRWGVFSGRTPPSRYNFDWWYL	500
451	DIESDINYLKMALEKIAFLPFGYLVDQWRWGVFSGRTPPSRYNFDWWYL	500

**FIG. 57 (CONT.)**

```

501 RTKYQGICPPVARNETHFDAGAKFHIPNVTPIRYFVSFVLQFQHQAALC 550
|||||
501 RTKYQGICPPVARNETHFDAGAKFHIPNVTPIRYFVSFVLQFQHQAALC 550

551 KEAGHQGPLHQCDIYQSXAQAKLKQVLQAGCSRWPQEVKDLVGSDALD 600
|||||
551 KEAGHQGPLHQCDIYQSTQAGAKLKQVLQAGCSRWPQEVKDLVGSDALD 600

601 AKALLEYFQVSQWLEEQNQRNGEVLGWPENQWRPPLPDNYPEGIDLETD 650
|||||
601 AKALLEYFQVSQWLEEQNQRNGEVLGWPENQWRPPLPDNYPEGIDLETD 650

651 EAKADRFVEEYDRTAQVLLNEYAEANWQYNTNITIEGSKILLEKSTEVS 700
|||||
651 EAKADRFVEEYDRTAQVLLNEYAEANWQYNTNITIEGSKILLEKSTEVS 700

701 HTLKYGTRAKTFDVSNFQNSSIKRIKKLQNLDRVLPKPKELEEYNQIILL 750
|||||
701 HTLKYGTRAKTFDVSNFQNSSIKRIKKLQNLDRVLPKPKELEEYNQIILL 750

```

**FIG. 57 (CONT.)**

751	DMETYSLSNICYTNGTCMPLEPDLTNMMATSRKYEEELLWAWKSWRDKVG	800
751	DMETYSLSNICYTNGTCMPLEPDLTNMMATSRKYEEELLWAWKSWRDKVG	800
801	RAILPFFPKYVEEFSNKIAKLNQYTDAGDSWRSLYESDNLEQDLEKLYQEL	850
801	RAILPFFPKYVEEFSNKIAKLNQYTDAGDSWRSLYESDNLEQDLEKLYQEL	850
851	QPLYLNLHAYVRRSLHRHYGSEYINLDGPIPAHLLGNMWAQTWSNIYDLV	900
851	QPLYLNLHAYVRRSLHRHYGSEYINLDGPIPAHLLGNMWAQTWSNIYDLV	900
901	APFPSAPNIDATEAMIKQGWTPRRIFKEADNFFTSGLLLPVPPEFWNKSM	950
901	APFPSAPNIDATEAMIKQGWTPRRIFKEADNFFTSGLLLPVPPEFWNKSM	950
951	LEKPTDGREVVCHPSAWDFYNGKDFRIKQCTSVNMEDLVIAHHEMIGHIQY	1000
951	LEKPTDGREVVCHPSAWDFYNGKDFRIKQCTSVNMEDLVIAHHEMIGHIQY	1000

FIG. 57 (CONT.)<sup>3</sup>

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1001 FMQYKDLPVTFREGANPGFHEAIGDIMALSVSTPKHLYSLNLLSTEGSY 1050  
|||||  
1001 FMQYKDLPVTFREGANPGFHEAIGDIMALSVSTPKHLYSLNLLSTEGSY 1050  
|||||  
1051 EYDINFLMKMALDKIAFIPFSYLIDQWRWRVFDGSITKENYNQEWWSLRL 1100  
|||||  
1051 EYDINFLMKMALDKIAFIPFSYLIDQWRWRVFDGSITKENYNQEWWSLRL 1100  
|||||  
1101 KYQGLCPPVPRSQGDGDFGSKFHV PANVPYVRYFVSFIIQFQFHEALCRA 1150  
|||||  
1101 KYQGLCPPVPRSQGDGDFGSKFHV PANVPYVRYFVSFIIQFQFHEALCRA 1150  
|||||  
1151 AGHTGPLHKCDIYQSKEAGKLLADAMKLGYSKPWPEAMKLITGQPNMSAS 1200  
|||||  
1151 AGHTGPLHKCDIYQSKEAGKLLADAMKLGYSKPWPEAMKLITGQPNMSAS 1200  
|||||  
1201 AMMNYFKPLTEWLVTENRRRHGETL GWPEYNWAPNT 1235  
|||||  
1201 AMMNYFKPLTEWLVTENRRRHGETL GWPEYNWAPNT 1235

FIG. 57 (CONT. 4)

```

1 MTMTLHTKASGMALLHQIQGNELEPLNRPQLKMPMERALGEVYVDNSKPT 50
  |||||
1 MTMTLHTKASGMALLHQIQGNELEPLNRPQLKMPMERALGEVYVDNSKPT 50

51 VFNYPEGAAAYEFNAAAAAASAPVYQSGIAYGPGSEAAAFSANSLSGA 100
  |||||
51 VFNYPEGAAAYEFNAAAAAASAPVYQSGIAYGPGSEAAAFSANSLSGA 100

101 FPQLNSVSPSPLMLLHPPQLSPFLHPHGQQVPYYLENEPSAYAVRDTGP 150
  |||||
101 FPQLNSVSPSPLMLLHPPQLSPFLHPHGQQVPYYLENEPSAYAVRDTGP 150

151 PAFYRSNSDNRNRQNGRERLSSSNEKGNMIMESAKETRYCAVCNDYASGYH 200
  |||||
151 PAFYRSNSDNRNRQNGRERLSSSNEKGNMIMESAKETRYCAVCNDYASGYH 200

```

**FIG. 58**

201 YGVWSCEGCKAFFKRSIQGHNDYMC PATNQCTIDKNRRKSCQACRLKCY 250  
 |||||  
 201 YGVWSCEGCKAFFKRSIQGHNDYMC PATNQCTIDKNRRKSCQACRLKCY 250  
 |||||  
 251 EVGMMKGGIRKDRRGG RMLKHKRQRDDLEGRNEMGASGDMRAANLWP SPL 300  
 |||||  
 251 EVGMMKGGIRKDRRGG RMLKHKRQRDDLEGRNEMGASGDMRAANLWP SPL 300  
 |||||  
 301 VIKHTKKNSPALSLTADQMVSALLDAEPPMIYSEYDPSRPFSEASMMGLL 350  
 |||||  
 301 VIKHTKKNSPALSLTADQMVSALLDAEPPMIYSEYDPSRPFSEASMMGLL 350  
 |||||  
 351 TNLADREL VHMINWAKRVPG 370  
 |||||  
 351 TNLADREL VHMINWAKRVPG 370

**FIG. 58 (CONT. 1)**



```

1 MVPQAHGLLLCFLLQLQGPLGTAVFITQEEAHGVLHRQRANSLLLELW 50
  |||||
1 MVPQAHGLLLCFLLQLQGPLGTAVFITQEEAHGVLHRQRANSLLLELW 50
  |||||
51 PGSLERECNEEQCSFEEAREIFKSPERTKQFWIVYSDGDQACASNPCQNGG 100
  |||||
51 PGSLERECNEEQCSFEEAREIFKSPERTKQFWIVYSDGDQACASNPCQNGG 100
  |||||
101 TCQDHLKSYVCFCLLDFE..... 118
  |||||
101 TCQDHLKSYVCFCLLDFEGRNCEKSKNEQLICANENGDCDQYCRDHSVGTK 150
  |||||
119 .....GAVLLDARWIVTAAHCFDNIRYWG NITVVMG 149
  |||||
201 PKGECPWQAVL KINGLLCGAVLLDARWIVTAAHCFDNIRYWG NITVVMG 250
  |||||
150 EHDFSEKDGDEQVRRVTQVIMPDKYIRGKINHDIALLRLHRPVTFTDYVV 199
  |||||
251 EHDFSEKDGDEQVRRVTQVIMPDKYIRGKINHDIALLRLHRPVTFTDYVV 300
  |||||

```

65.51F

```
.      .      .      .      .  
200 PLCLPEKFSSENTLARI FSRVSGWGQLDRGATALELM SIEVPRLMTQD 249  
   |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  
301 PLCLPEKFSSENTLARI FSRVSGWGQLDRGATALELM SIEVPRLMTQD 350  
  
.      .      .      .      .  
250 CLEHAKHSNSTPKITENMFCAGYMDGTKDAC KDSGGPHATHYHG TWYLT 299  
   |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  
351 CLEHAKHSNSTPKITENMFCAGYMDGTKDAC KDSGGPHATHYHG TWYLT 400  
  
.      .      .      .      .  
300 GVVSWGEGCAAIGHIGVYTRVSQYIDWLVRHM DSKLQGVFRLPLL 345  
    |||||  |||||  |||||  |||||  |||||  |||||  |||||  |||||  
401 GVVSWGEGCAAIGHIGVYTRVSQYIDWLVRHM DSKLQGVFRLPLL 446
```

**FIG. 59 (CONT.)<sup>1</sup>**

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```

1 MGFLKFSPLVVSILL..... 17
  |||||
1 MGFLKFSPLVVSILLYQACSLQAVPLRSILESSPGMATLSEEEVRLLA 50

18 ALVQDYMQMKARELEQEEEEQEAEGSSLDSPRSKRCGNLSTCMLGTYTQDL 67
  |||||
51 ALVQDYMQMKARELEQEEEEQEAEGSSLDSPRSKRCGNLSTCMLGTYTQDL 100

      .
68 NKEHTFPQTSIGVEAPGKKRDVAKDLETNHQSHFGN 103
  |||||
101 NKEHTFPQTSIGVEAPGKKRDVAKDLETNHQSHFGN 136

```

**FIG. 60**

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1 MATLLRSKLTNVATSVSNKSQAKVSGMFARMGFQAATDEEAVGFAHCDDL 50  
|||||  
1 MATLLRSKLTNVATSVSNKSQAKVSGMFARMGFQAATDEEAVGFAHCDDL 50  
51 DFEHRQGLQMDILKSEGEPCGDEGAEPVEGDIHYQRGGAPLPPSGSKDQ 100  
|||||  
51 DFEHRQGLQMDILKSEGEPCGDEGAEPVEGDIHYQRGGAPLPPSGSKDQ 100  
101 AVGAGGEFGGHDKPKITAEAGWNVTNAIQGMFVLGLPYAILHGGYLGFL 150  
|||||  
101 AVGAGGEFGGHDKPKITAEAGWNVTNAIQGMFVLGLPYAILHGGYLGFL 150  
151 LIIFAAVVCCYTGKILIACLYEENEDGEVVRVSDSYVAIANACCAPRFT 200  
|||||  
151 LIIFAAVVCCYTGKILIACLYEENEDGEVVRVSDSYVAIANACCAPRFT 200  
201 LGGRVVNVAQIIELVMTCILYVVVSGNLMYNSFPGLPVSQKSWSIITAV 250  
|||||  
201 LGGRVVNVAQIIELVMTCILYVVVSGNLMYNSFPGLPVSQKSWSIITAV 250  
251 LLPCAFLKNLKA VSKFSLCTLAHFVINILVIA YCLSRARDWAEKVKFY 300  
|||||  
251 LLPCAFLKNLKA VSKFSLCTLAHFVINILVIA YCLSRARDWAEKVKFY 300

FIG. 61

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301 IDVKKFPISIGIIVFSYTSQIFLPSLEGNMQQPSEFHCMMNWTHIAACVL 350  
|||||  
301 IDVKKFPISIGIIVFSYTSQIFLPSLEGNMQQPSEFHCMMNWTHIAACVL 350  
351 KGLFALVAYLTWADETKEVITDNLPGSIRAVVNFLVAKALLSYPLPFFA 400  
|||||  
351 KGLFALVAYLTWADETKEVITDNLPGSIRAVVNFLVAKALLSYPLPFFA 400  
401 AVEVLEKSLFQEGSRAFFPACYGGDGRILKSWELTLRCALVVFTLLMAIYV 450  
|||||  
401 AVEVLEKSLFQEGSRAFFPACYGGDGRILKSWELTLRCALVVFTLLMAIYV 450  
451 PHFALLMGLTGSLTGAGLCFLLPSLFHLRLLWRKLLWHQVFFDVAFVIG 500  
|||||  
451 PHFALLMGLTGSLTGAGLCFLLPSLFHLRLLWRKLLWHQVFFDVAFVIG 500  
501 GICSVSGFVHSLEGLIEAYRT 521  
|||||  
501 GICSVSGFVHSLEGKFAGLET 521

FIG. 61 (CONT.<sup>1</sup>)

```

1 MDVLAENGTFALNLLKTLGKDNSKNVFFSPMSMSCALAMVYMGAKGNTA 50
  |||||
1 MDVLAENGTFALNLLKTLGKDNSKNVFFSPMSMSCALAMVYMGAKGNTA 50

51 AQMAQILSFNKSGGGDIHQGFQSLLTEVNKTGTQYLLRVANRLFGEKSC 100
  |||||
51 AQMAQILSFNKSGGGDIHQGFQSLLTEVNKTGTQYLLRVANRLFGEKSC 100

1101 DFLSSFRDSCQKFYQAEEMEELDFISAVEKSRKHINTWVAEKTEGKIAELL 150
  |||||
1101 DFLSSFRDSCQKFYQAEEMEELDFISAVEKSRKHINTWVAEKTEGKIAELL 150

1151 SPGSVDPLTRLVLVNAVYFRGNWDEQFDKENTEERLFKVSKNEEKPVQMM 200
  |||||
1151 SPGSVDPLTRLVLVNAVYFRGNWDGQFDKENTEERLFKVSKNEEKPVQMM 200

2201 FKQSTFKKTYIGEIFTQILVLVPYVGKELNMIIMLPDETDDLRTVEKELTY 250
  |||||
2201 FKQSTFKKTYIGEIFTQILVLVPYVGKELNMIIMLPDETDDLRTVEKELTY 250

```

**FIG. 62**

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251 EKFEWTRLDMMDEEEVEVSLPRFKLEESYDMESVLRNLGMTDAFELGKA 300  
|||||  
251 EKFEWTRLDMMDEEEVEVSLPRFKLEESYDMESVLRNLGMTDAFELGKA 300  
301 DFSGMSQTDLSLSKVVKHSFVEVNEEGTEAAAAATAAIMMRCARFVPRFC 350  
|||||  
301 DFSGMSQTDLSLSKVVKHSFVEVNEEGTEAAAAATAAIMMRCARFVPRFC 350  
351 ADHPFLFFIQHSKTNIGILFCGR 372  
|||||  
351 ADHPFLFFIQHRKTNIGILFCGR 372

FIG. 62 (CONT. <sup>1</sup>)

```

1 MDVLAEANGTFALNLLKTLGKDNSKNVFFSPMSMCSALAMVYMGAKGNTA 50
  |||||
1 MDVLAEANGTFALNLLKTLGKDNSKNVFFSPMSMCSALAMVYMGAKGNTA 50

51 AQMAQILSFNKSGGGDIHQGFQSLLTEVNKTGTQYLLRVANRLFGEKSC 100
  |||||
51 AQMAQILSFNKSGGGDIHQGFQSLLTEVNKTGTQYLLRVANRLFGEKSC 100

101 DFLSSFRDSCQKFYQAEEMEELDFISAVEKSRKHINTWVAEKTEGKIAELL 150
  |||||
101 DFLSSFRDSCQKFYQAEEMEELDFISAVEKSRKHINTWVAEKTEGKIAELL 150

151 SPGSVDPLTRLVLNAVYFRGNWDEQFDKENTEERLFKVSKNEEKPVQMM 200
  |||||
151 SPGSVDPLTRLVLNAVYFRGNWDGQFDKENTEERLFKVSKNEEKPVQMM 200

201 FKQSTFKKTYIGEIFTQILVLPYVGKELNMIIMLPDETTDLRTVEKELTY 250
  |||||
201 FKQSTFKKTYIGEIFTQILVLPYVGKELNMIIMLPDETTDLRTVEKELTY 250

```

**FIG. 63**



FIG. 63 (CONT.<sup>1</sup>)

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157 VGYRVPAGSGPSLPPMPSLQEVDCGSPSSSEEEGVPGSRGSPATSPHLGR 206  
:|||||  
1 IGYRVPAGSGPSLPPMPSLQEVDCGSPSSSEEEGVPGSRGSPATSPHLGR 50

207 RRPLLRMSA AFCSL LAPERQV GRAAAALMQDRHTAAGQLVQDLLTQVRD 256  
|||||  
51 RRPLLRMSA AFCSL LAPERQV GRAAAALMQDRHTAAGQLVQDLLTQVRD 100

257 GORPQEEGIRQALSRARAMLSAELGPEKLVSPKRLEHVLEKSLHCSVLK 306  
|||||  
101 GORPQEEGIRQALSRARAMLSAELGPEKLVSPKRLEHVLEKSLHCSVLK 150

307 PLRPILAARLRRRLAADGSLGR LAEGLRLARAQGPAGFSGHLSLPSPVEL 356  
|||||  
151 PLRPILAARLRRRLAADGSLGR LAEGLRLARAQGPAGFSGHLSLPSPVEL 200

357 EQVRQKLLQLVRTYSPSAQVKRLLQACKLLYMALRTQEGEGSGADGFLPL 406  
|||||  
201 EQVRQKLLQLVRTYSPSAQVKRLLQACKLLYMALRTQEGEGSGADGFLPL 250

FIG. 64

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407 LSLVLAHCDLPELLLEAEYMSLELPSLLTGE GGYLTSLASLALLSGL 456  
|||||  
251 LSLVLAHCDLPELLLEAEYMSLELPSLLTGE GGYLTSLASLALLSGL 300  
|||||

457 GQAHTLPLSPVQELRRSLSLWEQRRLPATHCFQ 489  
|||||

301 GQAHTLPLSPVQELRRSLSLWEQRRLPATHCFQ 333  
|||||

FIG. 64 (CONT. <sup>1</sup>)

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122 MSDASLRSTMERLVARGTFPVLVRTSACRSLFGPVDHEELSRELQARL 171  
|||||  
1 MSDASLRSTMERLVARGTFPVLVRTSACRSLFGPVDHEELSRELQARL 50

172 AELNAEDQNRWDYDFQQDMPLRGPGRLQWTEVDSVPAFYRETQVVGRC 221  
|||||  
51 AELNAEDQNRWDYDFQQDMPLRGPGRLQWTEVDSVPAFYRETQVVGRC 100

222 RLLAPRPVAVAVAVSPPLEPAAESLDGLEEAPEQLPSVPVPAPASTPPP 271  
|||||  
101 RLLAPRPVAVAVAVSPPLEPAAESLDGLEEAPEQLPSVPVPAPASTPPP 150

272 VPVLAPAPAPAPAPVAAAPVAVPVLAPAPAPAPAPAPAPVAAAPAP 321  
|||||  
151 VPVLAPAPAPAPVAAAPVAVAVLAPAPAPAPAPAPAPVAAAPAP 200

322 APAPAPAPAPAPAPDAAPQESAEQGANQQGQGEPLADQLHSGISGRP 371  
|||||  
201 APAPAPAPAPAPAPDAAPQESAEQGANQQGQGEPLADQLHSGISGRP 250

FIG. 65

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372 AAGTAAASANGAAIKKLSGPLISDFFAKRKRSAPEKSSGSDVPAPCPSPSA 421  
|||||  
251 AAGTAAASANGAAIKKLSGPLISDFFAKRKRSAPEKSSGSDVPAPCPSPSA 300  
422 APGVGSVEQTPRKRLR 437  
|||||  
301 APGVGSVEQTPRKRLR 316

FIG. 65 (CONT.<sup>1</sup>)

```

1 MEPAAGSSMEPSADWLASAAARGLVEKVRQLLEAGADPNAPNSYGRRPIQ 50
  |||||
1 MEPAAGSSMEPSADWLASAAARGRVEEVRAALLEAGALPNAPNSYGRRPIQ 50
  . . . . .
51 VMMGSARVAELLLHGAEPNCADPATLTRPVHDAAREGFDTLVVLHRA 100
  |||||
51 VMMGSARVAELLLHGAEPNCADPATLTRPVHDAAREGFDTLVVLHRA 100
  . . . . .
101 GARLDVRDAWGRLPVDLAEELGHRDVARYLRAAAGGTRGSNHARIDAAEG 150
  |||||
101 GARLDVRDAWGRLPVDLAEELGHRDVARYLRAAAGGTRGSNHARIDAAEG 150
  151 PS 152
  ||
  151 PS 152

```

FIG. 66

```

1 MREENKMPSGGSGDEGLASAAARGLVEKVRQLLLEAGADPNGVNRFGRR 50
  | | | | | | | | | | | | | | | | | | | | | | | | | | | |
1 MREENKMPSGGSGDEGLASAAARGLVEKVRQLLLEAGADPNGVNRFGRR 50

51 IQVMMMG SARVAELLLHGAEPNCADPATLTRPVHDAAREGEFDTLVVLH 100
  | | | | | | | | | | | | | | | | | | | | | | | | | | | |
51 IQVMMMG SARVAELLLHGAEPNCADPATLTRPVHDAAREGEFDTLVVLH 100

      .      .      .      .
101 RAGARLDVRDAWGRLPVDLAEELGHRDVARYLRAAAG 137
   | | | | | | | | | | | | | | | | | | | | | |
101 RAGARLDVRDAWGRLPVDLAEERGHRDVAGYLRTATG 137

```

**FIG. 67**

```

1 MKHSLNALLIFLIITSAWGSGKGPLDQLEKGGETAQSA DPQEQLNNKNL 50
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
1 MKHSLNALLIFLIITSAWGSGKGPLDQLEKGGETAQSA DPQEQLNNKNL 50

51 SMPLLPADFH KENTVTNDWIPEGEEDDDYLDLEKIFSEDDDYIDIVDSL S 100
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
51 SMPLLPADFH KENTVTNDWIPEGEEDDDYLDLEKIFSEDDDYIDIVDSL S 100

101 VSPTSDVSAGNILQLFHGKSRIQRNLINAKFAFNLYRV LKDQVNTFDN 150
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
101 VSPTSDVSAGNILQLFHGKSRIQRNLINAKFAFNLYRV LKDQVNTFDN 150

151 IFIAPVGISTAMGMISGLKGETHEQVHSILHF KD FVNASSKY EITTIHN 200
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
151 IFIAPVGISTAMGMISGLKGETHEQVHSILHF KD FVNASSKY EITTIHN 200

201 LFRKLTHRLFRRNFGYTLRS VNDLYIQKFPI LLDFKT KVREYYFAE AQI 250
| | | | | | | | | | | | | | | | | | | | | | | | | | | |
201 LFRKLTHRLFRRNFGYTLRS VNDLYIQKFPI LLDFKT KVREYYFAE AQI 250

```

FIG. 89



[illegible]

FIG. 68 (CONT. 1)

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1 MDPARPLGLSILLFLTEAALGDAAQEPTGNNAEICLLPLDYGPCRALLL 50  
|||||  
1 MDPARPLGLSILLFLTEAALGDAAQEPTGNNAEICLLPLDYGPCRALLL 50

51 RYYDRYTQSCRQFLYGGCEGNANNFYTWEACDDACWRIEKVPKVCRLQV 100  
|||||  
51 RYYDRYTQSCRQFLYGGCEGNANNFYTWEACDDACWRIEKVPKVCRLQV 100

101 SVDDQCEGSTEKYFFNLSSMTCEKFFSGGCHRNRIENRFPDEATCMGFCA 150  
|||||  
101 SVDDQCEGSTEKYFFNLSSMTCEKFFSGGCHRNRIENRFPDEATCMGFCA 150

151 PKKIPSFYCSPKDEGLCSANVTRYFNPRTCDAFYTGCGGNDNNFVT 200  
|||||  
151 PKKIPSFYCSPKDEGLCSANVTRYFNPRTCDAFYTGCGGNDNNFVS 200

201 VQK.MRDCA 208  
: | ||  
201 REDCKRACA 209

FIG. 69

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```

1 MDPARPLGLSILLFLTEAALGDAQAQPTGNNAEICLLPLDYGPCRALLL 50
  |||||
1 MDPARPLGLSILLFLTEAALGDAQAQPTGNNAEICLLPLDYGPCRALLL 50

51 RYYYDRYTQSCRQFLYGGCEGNANNFYTWACDDACWRIEKVPKVCRLQV 100
  |||||
51 RYYYDRYTQSCRQFLYGGCEGNANNFYTWACDDACWRIEKVPKVCRLQV 100

101 SVDDQCEGSTEKYFFNLSSMTCEKFFSGGCHRNRIENRFPDEATCMGFCA 150
  |||||
101 SVDDQCEGSTEKYFFNLSSMTCEKFFSGGCHRNRIENRFPDEATCMGFCA 150

151 PKK.....KYRTCDAFTYTGCGGNDNNFVS 175
  |||:|||||

151 PKKIPSFYCSPKDEGLCSANVTRYFNPRTCDFTYTGCGGNDNNFVS 200
  .
176 REDCKRACAKALKKKKMPKLRFASRIRKIRKKQF 210
  |||||
201 REDCKRACAKALKKKKMPKLRFASRIRKIRKKQF 235

```

FIG. 70



1 MASRLTLTLLLLLAGDRASSNP NATSSSSQDPESLQDRGEGKVATTVI 50  
 1 MASRLTLTLLLLLAGDRASSNP NATSSSSQDPESLQDRGEGKVATTVI 50  
 51 SKMLFVEPILEVSSLPTTNSTTNSATKITANTTDEPTTQPTTEPTTQPTI 100  
 51 SKMLFVEPILEVSSLPTTNSTTNSATKITANTTDEPTTQPTTEPTTQPTI 100  
 101 QPTQPTTQLPTDSTPTQPTTGSGFCPGPVTLCSDLESHSTEAVLGDALVDFS 150  
 101 QPTQPTTQLPTDSTPTQPTTGSGFCPGPVTLCSDLESHSTEAVLGDALVDFS 150  
 1151 LKLYHAFSAMKKVETNMAFSPFSIASLLTQVLLGAGENTKTNLESILSYP 200  
 1151 LKLYHAFSAMKKVETNMAFSPFSIASLLTQVLLGAGENTKTNLESILSYP 200

**FIG. 72**

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201 KDFTCVHQALKGFTTKGVTSVSQIFHSPVDWRLLQSKSQEVLSQTSTKAR 250

|||||

201 KDFTCVHQALKGFTTKGVTSVSQIFHS..... 227

.  
.  
.

351 VERTYCFPEFLKYPDDLAIKRTFVNASRTLYSSSPRVLSNNSDANLELINT 400

|||||

228 ..... PDLAIRDTFVNASRTLYSSSPRVLSNNSDANLELINT 264

401 WVAKNTNNKISRLLDSPDTRLVLLNAIYLSAKWKTFDPPKTRMEPFH 450

|||||

265 WVAKNTNNKISRLLDSPDTRLVLLNAIYLSAKWKTFDPPKTRMEPFH 314

451 FKNSVIKVPMMNSKKYPVAHFIDQTLKAKVGQLQLSHNLSLVLPQNLK 500

|||||

315 FKNSVIKVPMMNSKKYPVAHFIDQTLKAKVGQLQLSHNLSLVLPQNLK 364

.  
.  
.

FIG. 72 (CONT. <sup>1</sup>)

```

501 HRLDMEQALSPSVFKAIMKLEMSKFQPTLLTPRIKVTTSQDMLSIME 550
    |||||
365 HRLDMEQALSPSVFKAIMKLEMSKFQPTLLTPRIKVTTSQDMLSIME 414
    |||||
551 KLEFFDFSYDLNLCGLTEDPDLQVSAMQHQTVLELTETGVEAAAAAISV 600
    |||||
415 KLEFFDFSYDLNLCGLTEDPDLQVSAMQHQTVLELTETGVEAAAAAISV 464
    |||||
    .
601 ARTLLVFEVQQPFLEVLWDQQHKFPVFMGRVYDPRA 636
    |||||
465 ARTLLVFEVQQPFLEVLWDQQHKFPVFMGRVYDPRA 500

```

**FIG. 72 (CONT. 2)**

[illegible]

**FIG. 73**







```

1 MDVLAEANGTFAINLLKTLGKDNSKNVFFSPMSCALAMVYMGAKNTA 50
  |||||
1 MDVLAEANGTFAINLLKTLGKDNSKNVFFSPMSCALAMVYMGAKNTA 50

51 AQMAQILSFNKSGGGDIHQGFQSLLTEVNKTGTQYLLRMANRLFGEKSC 100
  |||||
51 AQMAQILSFNKSGGGDIHQGFQSLLTEVNKTGTQYLLRMANRLFGEKSC 100

101 DFLSSFRDSCQKFYQAEMEELDFISAVEKSRKHINTWVAEKTEGKM 146
  |||||
101 DFLSSFRDSCQKFYQAEMEELDFISAVEKSRKHINTWVAEKTEGKI 146

```

[illegible]

**FIG. 76**

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```

      .      .      .      .      .
301 DLRDLVTTLGGALLWLSGHAGTQAQGAARVAAALDDGSALGRFERMLAAQ 350
      |||||
301 DLRDLVTTLGGALLWLSGHAGTQAQGAARVAAALDDGSALGRFERMLAAQ 350

      .      .      .      .      .
351 GVDPGALARALCSGSPAERRQLLPRAREQEELLAPADGERSGESPSFRLRH 400
      |||||
351 GVDPGALARALCSGSPAERRQLLPRAREQEELLAPAD..... 386

      .      .      .      .      .
401 PLPFRPRPFPSRPLSAPLPAGTVELVRALPLALVLHELGAGRSRAGEPL 450
      |||||
387 .....GTVELVRALPLALVLHELGAGRSRAGEPL 415

      .      .      .      .      .
451 RLGVGAEILLVDVGQRLRRGTPWLRVHRDGPALSGPQSRALQEALVLSdra 500
      |||||
416 RLGVGAEILLVDVGQRLRRGTPWLRVHRDGPALSGPQSRALQEALVLSdra 465

      .
501 PFAAPSPFAELVLPPQQ 517
      |||||
466 PFAAPSPFAELVLPPQQ 482

```

FIG. 76 (CONT.<sup>1</sup>)





301	DGTPYVTVLKTAGANTTDKELEVL	SLHNVT	FEDAGEY	TCLAGNSIG	FSHH	350		
301	DGTPYVTVLKTAGANTTDKELEVL	SLHNVT	FEDAGEY	TCLAGNSIG	FSHH	350		
351	SAWL	VVLP	PAEEEL	VEADEAGSVYAGILSYGVGF	FLVVA	AVTXCRLRS 400		
351	SAWL	VVLP	PAEEEL	VEADEAGSVYAGILSYGVGF	FLVVA	AVTLCRLRS 400		
401	PPKKG	LGSP	TVHKIS	RFP	LKRQV	SLASN	SSNTPLVRIARLSSGEGPT 450	
401	PPKKG	LGSP	TVHKIS	RFP	LKRQV	SLASN	SSNTPLVRIARLSSGEGPT 450	
451	LANV	SELE	L	PADP	KWEL	SRARL	TLGKPLGEGCFGVVMAE	AIGIDKDRAA 500
451	LANV	SELE	L	PADP	KWEL	SRARL	TLGKPLGEGCFGVVMAE	AIGIDKDRAA 500
501	KPVT	VAVK	MLKDD	ATDK	DLSD	LVSE	MEMMKMIGKHKNI	INLL 542
501	KPVT	VAVK	MLKDD	ATDK	DLSD	LVSE	MEMMKMIGKHKNI	INLL 542

**FIG. 78 (CONT. 1)**



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1 MDPARPLGLSILLFLTEAALGDAAQEPTGNNAEICLLPLDYGPCRALLL 50  
|||||  
1 MDPARPLGLSILLFLTEAALGDAAQEPTGNNAEICLLPLDYGPCRALLL 50  
51 RYYYDRYTQSCRQFLYGGCEGNNNFYTWEACDDACWRIEKVPKVCRLQV 100  
|||||  
51 RYYYDRYTQSCRQFLYGGCEGNANNFYTWEACDDACWRIEKVPKVCRLQV 100  
101 SVDDQCEGSTEKYFFNLSSMTCEKFFSGGCHRNRIENRFPDEATCMGFCA 150  
|||||  
101 SVDDQCEGSTEKYFFNLSSMTCEKFFSGGCHRNRIENRFPDEATCMGFCA 150  
151 PKKIPSECYSPKDEGLCSANVTRYFN 177  
|||||  
151 PKKIPSECYSPKDEGLCSANVTRYFN 177

FIG. 79

```

1 MNQLRGKKSCHTGLGRSAGWNIPIGLLYCDLPEPRKPLEKAVANFFSGSC 50
  |||||
1 MNQLRGKKSCHTGLGRSAGWNIPIGLLYCDLPEPRKPLEKAVANFFSGSC 50

51 APCADGTDFPQLCQLCPGCGCSTLNQYFGYSGAFKCLKDGAGDVAFVKHS 100
  |||||
51 APCADGTDFPQLCQLCPGCGCSTLNQYFGYSGAFKCLKDGAGDVAFVKHS 100

101 TIFENLANKADRDQYELLCLDNTRKPVDEYKDKCHLAQVPSHTVVARSMSG 150
  |||||
101 TIFENLANKADRDQYELLCLDNTRKPVDEYKDKCHLAQVPSHTVVARSMSG 150

151 KEDLIWELLNQAQEHFGKDKSKEFQLFSSPHGKDLLFKDSAHGFLKVP 200
  |||||
151 KEDLIWELLNQAQEHFGKDKSKEFQLFSSPHGKDLLFKDSAHGFLKVP 200

201 MDAKMYLGYEYVTAIRNLREGTCPEAPTDECKPVKWCALSHHERLKCDEW 250
  |||||
201 MDAKMYLGYEYVTAIRNLREGTCPEAPTDECKPVKWCALSHHERLKCDEW 250

```

FIG. 80

```

251 SVNSVGKIECVSAETTEDCIAKIMNGEADAMSLDGGFVYIAGKCGLVPVL 300
    |||||
251 SVNSVGKIECVSAETTEDCIAKIMNGEADAMSLDGGFVYIAGKCGLVPVL 300

301 AENYNKSDNCEDTPEAGYFAVAVVKKSASDLTWDNLKGKKSCHTAVGRTA 350
    |||||
301 AENYNKSDNCEDTPEAGYFAVAVVKKSASDLTWDNLKGKKSCHTAVGRTA 350

351 GWNIPMGLLYNKINH.....CEP 368
    |||||
351 GWNIPMGLLYNKINHCRFDEFFSEGCAPGSKKDSLCKLCMGSGNLCEP 400

369 NNKEGYGYGTGAFRCLVEKGDVAFVKHQTVPQNTGGKNPDPWAKNLNEKD 418
    |||||
401 NNKEGYGYGTGAFRCLVEKGDVAFVKHQTVPQNTGGKNPDPWAKNLNEKD 450

419 YELLCLDGTRKPVVEEYANCHLARAPNHAVVTRKDKEACVHKILRQQQHLE 468
    |||||
451 YELLCLDGTRKPVVEEYANCHLARAPNHAVVTRKDKEACVHKILRQQQHLE 500
    . . . . .

```

FIG. 80 (CONT. <sup>1</sup>)

469 GSNVTDCSGNFC LFRSETKD L LFRDDTVCLAKLHNRNTYEKYLGE EYVKA 518  
|||||  
501 GSNVTDCSGNFC LFRSETKD L LFRDDTVCLAKLHNRNTYEKYLGE EYVKA 550  
519 VGNLRKCS TSS LLEACTFRRP 539  
|||||  
551 VGNLRKCS TSS LLEACTFRRP 571

FIG. 80 (CONT. <sup>2</sup>)



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37 NGFQVDNYGTQLNAVNNSLTPQSTKVPSLFEFHGPSWCLTPADRGLCRAN 86  
|||||  
180 NGFQVDNYGTQLNAVNNSLTPQSTKVPSLFEFHGPSWCLTPADRGLCRAN 229  
87 ENRFYNSVIGKCRPFKYSGCGGNENNFTSKQECRLACKKGFQIRISKGG 136  
|||||  
230 ENRFYNSVIGKCRPFKYSGCGGNENNFTSKQECRLACKKGFQIRISKGG 279  
137 LIKTKRKRKKQVRVKIAYEEIFVKNM 161  
|||||  
280 LIKTKRKRKKQVRVKIAYEEIFVKNM 304

FIG. 82

```

13 RPILTIITLEDSSGNLLGRDSFEVRCASPGDRPTEE 50
   |||||
246 RPILTIITLEDSSGNLLGRDSFEVRCACPGDRRTEE 283

51 ENFRKKEVLCPELPPGSAKRALPTCTSASPPQKKKPLDGEYFTLKIRGRK 100
   |||||
284 ENFRKKEVLCPELPPGSAKRALPTCTSASPPQKKKPLDGEYFTLKIRGRK 333

101 RFEMFRELNEALELKDAHATEESGDSRAHSSYLTKTKKGQSTSRHKKTMVK 150
   |||||
334 RFEMFRELNEALELKDAHATEESGDSRAHSSYLTKTKKGQSTSRHKKTMVK 383

151 KVGPDSD 157
   |||||
384 KVGPDSD 390

```

**FIG. 83**

```

13 RPILTIITLEDSSGNLLGRDSFEVRVCASPGRDPRTTE 50
|||||
246 RPILTIITLEDSSGNLLGRDSFEVRVCACPGRRRTTE 283

51 ENFRKKEVLCPELPPGSAKRALPTCTASPPQKKKPLDGEYFTLKIRGRK 100
|||||
284 ENFRKKEVLCPELPPGSAKRALPTCTASPPQKKKPLDGEYFTLKIRGRK 333

101 RFEMFRELNEALELKDAHATEESGDSRAHSSYLKTKKGQSTSRHKKTMTVK 150
|||||
334 RFEMFRELNEALELKDAHATEESGDSRAHSSYLKTKKGQSTSRHKKTMTVK 383

151 KVGPDSD 157
|||||
384 KVGPDSD 390

```

FIG. 84





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251	QLEPLYNLHAYVRRALHRRYGDKYVNLRGPIPAHLLGDMWAQSWENIYD	300
251	QLEPLYNLHAYVRRALHRRYGDKYVNLRGPIPAHLLGDMWAQSWENIYD	300
301	MVVPFPDKPNLDVTSTMVQKGWNATHMFRVSEEFFTSGLSPMPPEFWAE	350
301	MVVPFPDKPNLDVTSTMVQKGWNATHMFRVSEEFFTSGLSPMPPEFWAE	350
351	SMLEKPTDGREVVCHASAWDFYNRKDFRIKQCTRVTMEQLATVHHMGHV	400
351	SMLEKPTDGREVVCHASAWDFYNRKDFRIKQCTRVTMEQLATVHHMGHV	400
401	QYYLQYKDLHVSLRRGANPGFHEAIGDVLALSVSTPAHLHKIGLLDHVTN	450
401	QYYLQYKDLHVSLRRGANPGFHEAIGDVLALSVSTPAHLHKIGLLDHVTN	450
451	DIESDINYLKMALEKIAFLPFGYLVQDQWRWGVFSGRTPPSRYNFDWWYL	500
451	DIESDINYLKMALEKIAFLPFGYLVQDQWRWGVFSGRTPPSRYNFDWWYL	500

FIG. 85 (CONT.)<sup>1</sup>

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501 RTKYQGICPPVARNETHFDAGAKFHIPNVTPYIRYFVSFVLQFQHQAALC 550  
|||||  
501 RTKYQGICPPVARNETHFDAGAKFHIPNVTPYIRYFVSFVLQFQHQAALC 550  
|||||

551 KEAGHQGPLHQCDIYQSAQAGAKLKQVLQAGCSRQWQEVVKDLVGSDALD 600  
|||||  
551 KEAGHQGPLHQCDIYQSAQAGAKLKQVLQAGCSRQWQEVVKDLVGSDALD 600  
|||||

601 AKALLEYFQPVSQWLEEQNQRNGEVLGWPENQWRPPLPDNYPEGIDLETD 650  
|||||  
601 AKALLEYFQPVSQWLEEQNQRNGEVLGWPENQWRPPLPDNYPEGIDLETD 650  
|||||

651 EAKADRFVEEYDRTAQVLLNEYAEANWQYNTNITIEGSKILLEKSTEVSN 700  
|||||  
651 EAKADRFVEEYDRTAQVLLNEYAEANWQYNTNITIEGSKILLEKSTEVSN 700  
|||||

701 HTLKYGTRAKTFDVSNFQNSSIKRI IKKLQNLDR AVLPPKELEEYNQIILL 750  
|||||  
701 HTLKYGTRAKTFDVSNFQNSSIKRI IKKLQNLDR AVLPPKELEEYNQIILL 750  
|||||

751 DMETTYSLSNICYTNGTCMPLEPDLTNMMATSRKYEEELLWAWKSWRDKVG 800  
|||||  
751 DMETTYSLSNICYTNGTCMPLEPDLTNMMATSRKYEEELLWAWKSWRDKVG 800  
|||||

FIG. 85 (CONT. 2)

801	RAILPFFPKYVEFSNKIAKLNGYTDAGDSWRSLYESDNLEQDLEKLYQEL	850
801	RAILPFFPKYVEFSNKIAKLNGYTDAGDSWRSLYESDNLEQDLEKLYQEL	850
851	QPLYNLHAYVRRSLHRHYGSEYINLDGPIPAHLLGNMWAQTWSNIYDLV	900
851	QPLYNLHAYVRRSLHRHYGSEYINLDGPIPAHLLGNMWAQTWSNIYDLV	900
901	APFPSAPNIDATEAMIKQGWTPRRIFKEADNFFTSGLLPVPPPEFWNKSM	950
901	APFPSAPNIDATEAMIKQGWTPRRIFKEADNFFTSGLLPVPPPEFWNKSM	950
951	LEKPTDGREVVCHPSAWDFYNGKDFRIKQCTSVNMEDLVIAHHEMIGHIQY	1000
951	LEKPTDGREVVCHPSAWDFYNGKDFRIKQCTSVNMEDLVIAHHEMIGHIQY	1000
1001	FMQYKDLPVTFREGANPGFHEAIGDIMALSVSTPKHLYSLNLLSTEGSGY	1050
1001	FMQYKDLPVTFREGANPGFHEAIGDIMALSVSTPKHLYSLNLLSTEGSGY	1050

**FIG. 85 (CONT. <sup>3</sup>)**

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1051 EYDINFLMKMALKIAFIPFSYLIDQWRWRVFDGSITKENYNQEWWSLRL 1100  
|||||  
1051 EYDINFLMKMALKIAFIPFSYLIDQWRWRVFDGSITKENYNQEWWSLRL 1100  
|||||  
1101 KYQGLCPPVPRSQGFDPGSKFHV PANVPYRVYFVSFIIQFQFHEALCRA 1150  
|||||  
1101 KYQGLCPPVPRSQGFDPGSKFHV PANVPYRVYFVSFIIQFQFHEALCRA 1150  
|||||  
1151 AGHTGPLHKCDIYQSK EAGKLLADAMKLGYSKPWPEAMKLLITGQPNMSAS 1200  
|||||  
1151 AGHTGPLHKCDIYQSK EAGKLLADAMKLGYSKPWPEAMKLLITGQPNMSAS 1200  
|||||  
1201 AMMNYFKPLTEWLVTENRRRHGETL GWPEYNWAPNT 1235  
|||||  
1201 AMMNYFKPLTEWLVTENRRRHGETL GWPEYNWAPNT 1235

FIG. 85 (CONT. <sup>4</sup>)

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1 MTMTLHTKASGMALLHQIQGNELEPLNRPQLKMPMERALGEVYVDNSKPT 50  
|||||  
1 MTMTLHTKASGMALLHQIQGNELEPLNRPQLKMPMERALGEVYVDNSKPT 50

51 VFNYPEGAAYEFNAAAAAASAPVYQGSGIAYGPGSEAAAFSANSLSGA 100  
|||||  
51 VFNYPEGAAYEFNAAAAAASAPVYQGSGIAYGPGSEAAAFSANSLSGA 100

101 FPQLNSVSPSPMLLLHPPPPQLSPFLHPHGQQVPYYLENEPSAYAVRDTGP 150  
|||||  
101 FPQLNSVSPSPMLLLHPPPPQLSPFLHPHGQQVPYYLENEPSAYAVRDTGP 150

151 PAFYRSNSDNRRQNGRERLSSSNEKGNMIMESAKETRYCAVCNDYASGYH 200  
|||||  
151 PAFYRSNSDNRRQNGRERLSSSNEKGNMIMESAKETRYCAVCNDYASGYH 200

201 YGVWSCEGCKAFFKRSIQGHNDYMC PATNQCTIDKNRRKSCQACRLRKCY 250  
|||||  
201 YGVWSCEGCKAFFKRSIQGHNDYMC PATNQCTIDKNRRKSCQACRLRKCY 250

FIG. 86







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251 LLPCAFLKNLKAVSKFSLCTLAHFVINILVIAAYCLSRARDWAEKVKFY 300  
|||||  
251 LLPCAFLKNLKAVSKFSLCTLAHFVINILVIAAYCLSRARDWAEKVKFY 300  
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301 IDVKKFPISIGIIVFSYTSQIFLPSLEGNMQQSEFHCMMNWTHIAACVL 350  
351 KGLFALVAYLTWADETKEVITDNLPGSIRAVVNFLVAKALLSYPLPFFA 400  
|||||  
351 KGLFALVAYLTWADETKEVITDNLPGSIRAVVNFLVAKALLSYPLPFFA 400  
401 AVEVLEKSLFQEGSRAFFPACYGGDGRKLSWGLTLRCALVVFLLMAI 448  
|||||  
401 AVEVLEKSLFQEGSRAFFPACYGGDGRKLSWGLTLRCALVVFLLMAI 448

FIG. 87 (CONT. <sup>1</sup>)

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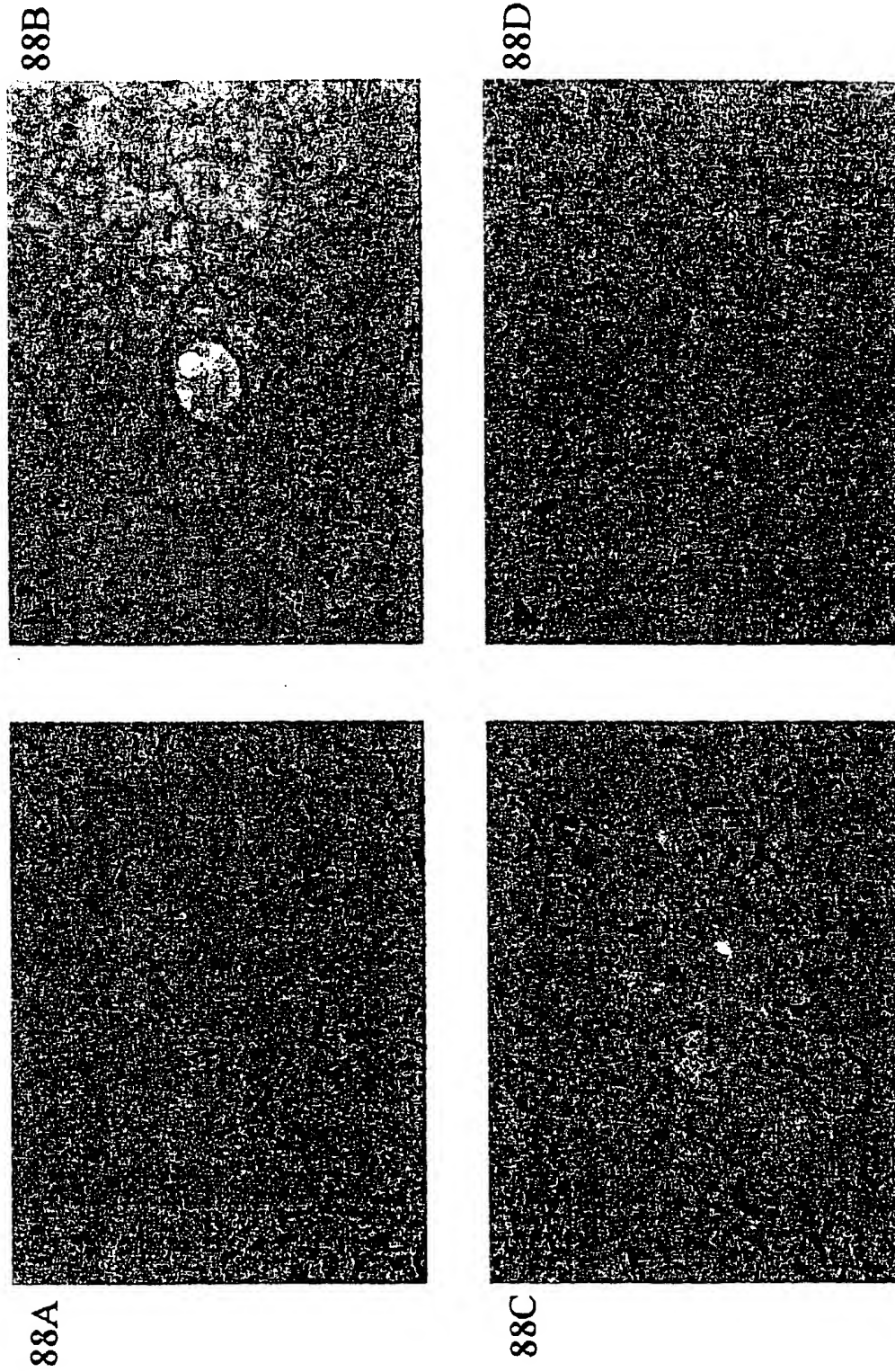
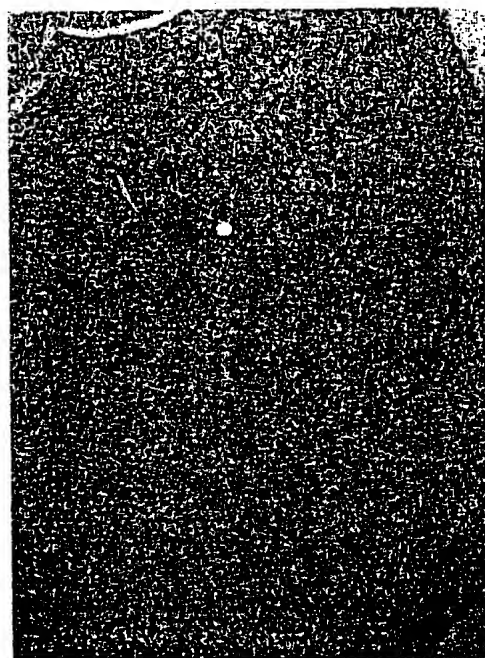
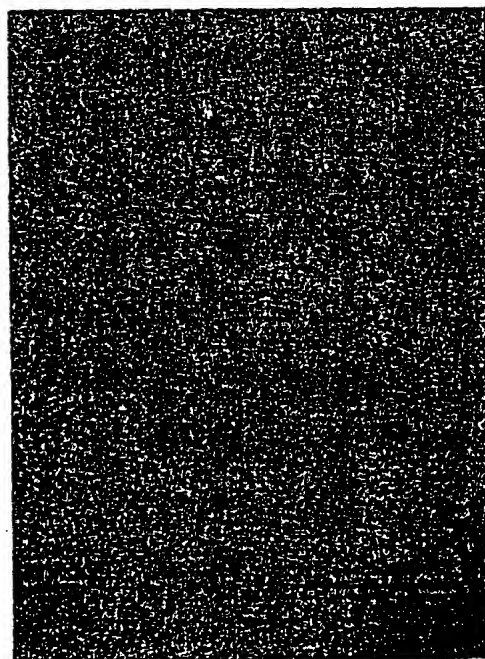


FIG. 88

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89B



89A

FIG. 89

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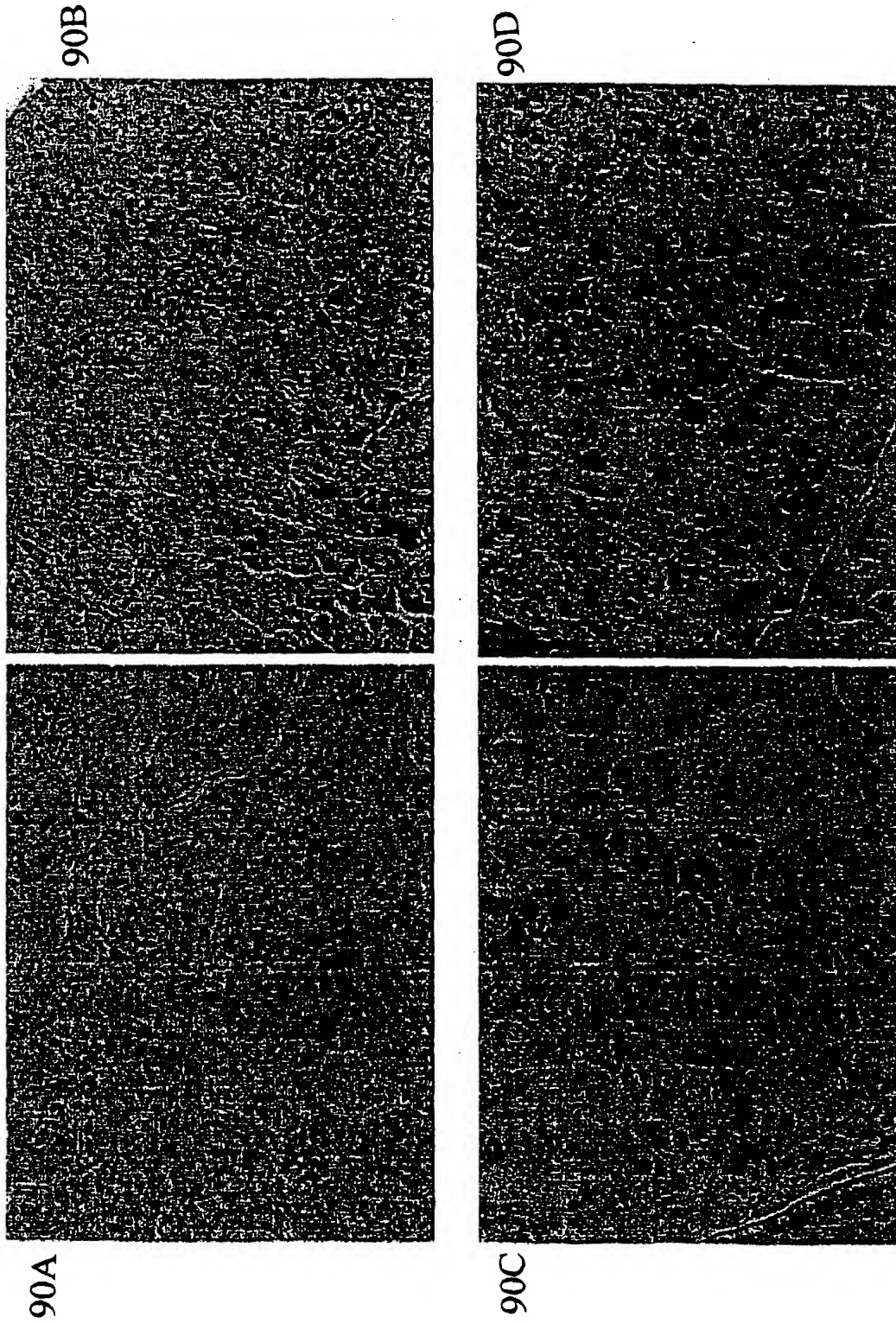


FIG. 90

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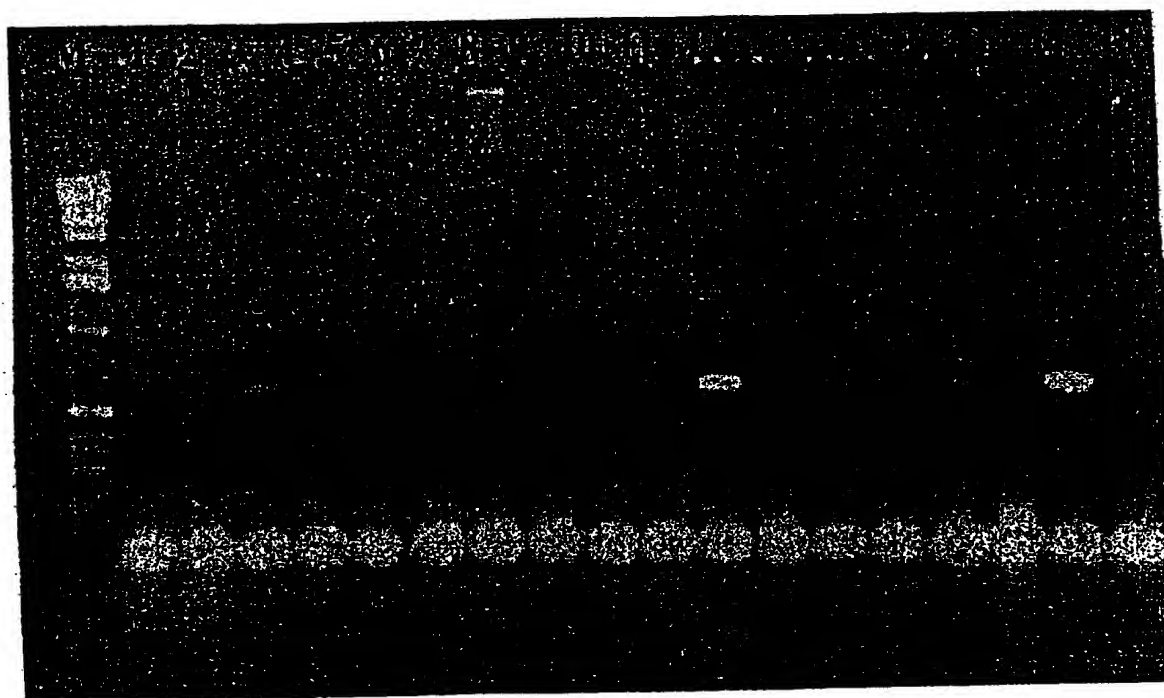
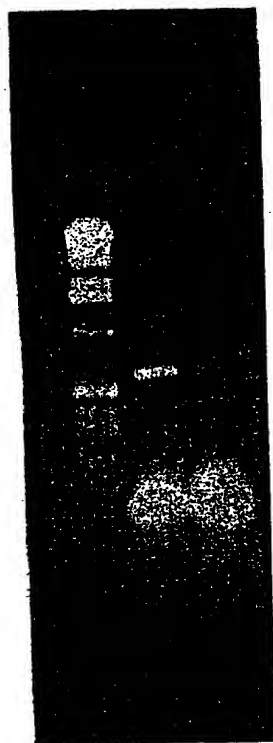


FIG. 91A

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Liver RT+  
Liver RT-  
Skin RT+  
Skin RT-  
Thyroid RT+  
Thyroid RT-  
Bone marrow  
RT+  
Bone marrow RT-  
Salivary gland  
RT+  
Salivary gland  
RT-  
Lung RT+  
Lung RT-  
Heart RT+  
Heart RT-  
Thymus RT+  
Thymus RT-  
Spleen RT+  
Spleen RT-  
Brain RT+  
Brain RT-

FIG. 91B

## SEQUENCE LISTING

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&lt;120&gt; VARIANTS OF ALTERNATIVE SPLICING

&lt;130&gt; 1293240-COMPUGEN

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&lt;151&gt; 1999-11-17

&lt;150&gt; IL133455

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&lt;160&gt; 174

&lt;170&gt; PatentIn Ver. 2.1

&lt;210&gt; 1

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

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cgcagcttta aggagttcct gcagtcacagc ctgagggctc ttcggcaaat gtagcatggg 540
cacctcagat tgttggtgtt aatgggcatt ccttcttctg gtcagaaacc tgtccactgg 600
gcacagaact tatgttggtt tctatggaga actaaaagta tgagcgtagt gacactatct 660
taattatttt taattttatta atattttaa atgtgaagct gagttaattt atgtaagtca 720
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gtgtaggctt acctcaaata aatggctaac ttatacatat ttttaagaa atatttatat 900
tgtatttata taatgtataa atgggtttta taccaataaa tggcatttta aaaaattcag 960
caaaaaa

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&lt;210&gt; 11

&lt;211&gt; 948

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 11

```

atgcctcgcc tgttcttggt ccacctgcta graktctggt tactactgaa ccaattttcc 60
agagcagtcg cggmcwmatg gawggasgaw gttattaaat tatgcggccg cgaattagtt 120
cgcgcgcaga ttgccatttg cggcatgagc acctggagca aaaggtctct gagccaggaa 180
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&lt;210&gt; 12

&lt;211&gt; 703

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 12

```

ttcccccccc ccccccccc ccccgccccg gcacaggaca cagctgggtt ctgaagcttc 60
tgagttctgc agcctcacct ctgagaaaac ctcttttcca ccaataccat gaagctctgc 120
gtgactgtcc tgtctctcct catgctagta gctgccttct gctctccagc gctctcagca 180
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aactgaactg agctgctcag agacaggaag tcttcaggga aggtcacctg agcccggatg 420
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```

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ctcttaattt aatctttttt atgtgccgtg ttattgtatt aggtgtcatt tccattattt 540
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ctgctgttgc aaatacatgg ataacacatt tgattctgtg tgttttcata ataaaacttt 660
aaaataatgg aatgaacaa cctaatacaa taacacggca cat 703

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&lt;210&gt; 13

&lt;211&gt; 2468

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 13

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gcaccaacag ctccaccatg gggctggcct ggggactagg cgtcctgttc ctgatgcatg 180
tgtgtggcac caaccgcatt ccagagtctg gcggagacaa cagcgtgttt gacatctttg 240
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ctgggcat 2468

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&lt;210&gt; 14

&lt;211&gt; 1850

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens



&lt;400&gt; 14

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gcacgagcng aggtagaggt tgctcctgac gcacaggcat tccccgcgcc cctccagccc 60
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gatgaaacga cccaggagct ttgctctttt actgaatgct gcagtcagca 1850

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&lt;210&gt; 15

&lt;211&gt; 1771

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 15

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gcaccaacag ctccaccatg gggctggcct ggggactagg cgtcctgttc ctgatgcatg 180
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gaaaaacaaa ttcacctttt cccagctttt ttttccttgt gttcagggga ggcagaggtt 1740
ttttgaacgg gttaggggat tttgcaagt t 1771

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&lt;210&gt; 16

&lt;211&gt; 1750

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 16

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tcgcccgcct cgccaccgct cccggccgcc gcgtccggt acacacagga tccctgctgg 120
gcaccaacag ctccaccatg gggctggcct ggggactagg cgtcctgttc ctgatgcatg 180
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&lt;210&gt; 17

&lt;211&gt; 2101

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 17

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a 2101

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&lt;210&gt; 18

&lt;211&gt; 2339

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 18

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&lt;210&gt; 19

&lt;211&gt; 1982

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 19

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&lt;210&gt; 20

&lt;211&gt; 1804

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 20

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&lt;210&gt; 21

&lt;211&gt; 682

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 21

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acgagaagtt cgtagaatgg acgaggctgg acatgatgga tgaagaggag gtggaagtgt 180
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gaagtgggag cgattttttt tt                                     682

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&lt;210&gt; 22

&lt;211&gt; 1349

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 22

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ccaatctgaa gtgggagcga tttttttt 1349

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&lt;210&gt; 23

&lt;211&gt; 953

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 23

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&lt;210&gt; 24

&lt;211&gt; 498

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 24

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ggagatggta ataatcaggg ttgggtggag aatatctgag gaaactgcac ttgatttggg 120
ccttgaagag taattgactg gatttagatt tatctagaaa ggtcgttccc agcagaagca 180

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acaagaacaa caagcttgga ctgccatcat ggatgttttc gcagaagcaa atggcacctt 240
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catccatgat ggcagacctg gaacaagatt taaaatcagt atcacttaag cagcttcac 480
gcgactgcat ctcacgcg 498

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&lt;210&gt; 25

&lt;211&gt; 2291

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 25

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tgaattatat ttttaaaaca ttgaagagtt ttcagaaaga aggctagtag agttgattac 300
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&lt;210&gt; 26

&lt;211&gt; 3450

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 26

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&lt;211&gt; 1679

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 30

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&lt;213&gt; Homo sapiens

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&lt;210&gt; 32

&lt;211&gt; 1134

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 32

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&lt;211&gt; 2243

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&lt;213&gt; Homo sapiens

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&lt;210&gt; 34

&lt;211&gt; 2446

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 34

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&lt;210&gt; 35

&lt;211&gt; 886

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 35

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&lt;210&gt; 36

&lt;211&gt; 3050

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 36

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&lt;210&gt; 37

&lt;211&gt; 2254

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 37

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&lt;210&gt; 38



&lt;211&gt; 2199

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 38

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&lt;210&gt; 39

&lt;211&gt; 14800

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 39

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&lt;213&gt; Homo sapiens

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 1862

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;211&gt; 1922

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 50

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&lt;211&gt; 1208

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 51

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&lt;211&gt; 1194

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 52

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&lt;211&gt; 4334

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 53

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 54

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&lt;211&gt; 2842

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 55

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&lt;210&gt; 56

&lt;211&gt; 2243

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 56

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&lt;210&gt; 57

&lt;211&gt; 4563

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 57

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&lt;210&gt; 58

&lt;211&gt; 1630

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 58

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&lt;210&gt; 59

&lt;211&gt; 1551

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 59

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&lt;210&gt; 60

&lt;211&gt; 732

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 60

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<213> Homo sapiens

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<213> Homo sapiens

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&lt;211&gt; 1324

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 63

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&lt;211&gt; 2235

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 64

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&lt;211&gt; 1643

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;210&gt; 69

&lt;211&gt; 2308

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 69

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&lt;213&gt; Homo sapiens

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&lt;211&gt; 1091

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 71

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&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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&lt;213&gt; Homo sapiens

&lt;400&gt; 74

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cgcgccctgc aggaggcgt cgtactctcc gaccgcgcgc cattgcgcgc cccctcgccc 3240
ttcgcacagc tcttctgcc gccgcagcaa taaagctcct ttgccgcgaa aaaa 3294

```

&lt;210&gt; 77

&lt;211&gt; 902

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 77

```

gttgctgcta catgaacggt cccccaccgg acagccaggt agccgcgcgc tccctcgac 60
acgcagagtc gggcggcgcg ggggtctcct tgcgcccggc ctccgccttc tctctcttc 120
ctttccctt cttctcgtg tctctctctc tctcgtgccc cgcgtttgct cagccccggg 180
ccatgtccga cgcgtccctc cgcagcacat ccacgatgga gctcttctc gccgtggga 240
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agccaattta gagcccaaag agccccgagg gaacctgccg gggcagcgga cgttggagg 660
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catttatata aaatgtttaa tctctgctga aactcagtgc anacggcacg agggcctcgt 900
gc 902

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&lt;210&gt; 78

&lt;211&gt; 2052

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 78

```

ggggggcagc atgcccgcgc gcgctgcctg aggacgcgc ggcccccgcc cccgccatgg 60
gcgcccctgc ctgcgccctc gcgctctgcg tggcgcgtggc catcgtggcc ggccctcct 120
cggagtcctt ggggacggag cagcgcgtcg tggggcgagc ggcagaagtc ccggggccag 180
agccccggca gcaggagcag ttggtcttcg gcagcgggga tgctgtggag ctgagctgtc 240
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tgccctcgga gcgtgtcctg gtggggcccc agcggctgca ggtgctgaat gcctcccacg 360
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```

```

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ccggcaggtg cgattttgtt aaccacgcga cgaactttcc gaaaaataaa gacacctggt 2040
tgctaacctg aa 2052

```

&lt;210&gt; 79

&lt;211&gt; 1057

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 79

```

ggcacgagct cctcccgcga ggcgctttct cggacgcctt gccagcggg ccgcccagcc 60
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gaggtgtcac tgggcgatgc tgctcaggag ccaacaggaa ataacgcgga gatctgtctc 180
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```

&lt;210&gt; 80

&lt;211&gt; 2256

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 80

```

acggcgagcc tcactctccg ggtgcggcgc tgagcagcga gtncgactg tgctcgtg 60

```



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agtgggttgt gctaaccacg tctgtcttca cagctctgtg ttgccatgtg tgctgaacaa 2220
aaaataaaaa ttattattga ttttatattt caaaaa 2256

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&lt;210&gt; 81

&lt;211&gt; 632

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 81

```

gtgcattgag cgcgctccag ctgccgggac gagggggcg ccccccgcgt cggggcgctc 60
ggctacagct gcggggcccg aggtctccgc gactcgctc ccggcccatg ctggaggcgg 120
cggaaccgcg gggacctagg acggaggcgg cgggcgctgg gcggcccccg gcacgctgag 180
ctcgggatgc ggacgctgct gctcccgcg ctgctgacct gctggctgct cgcctccgtg 240
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attcacgccc gaggttttaa gaggatcctg gaccacata cctaccatt ggctccatga 420
ccagtgtctt tataattaca aaatcattga gaaattaagt cacaggaagc ctggtgtgtg 480
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agagtgtgtt tctccctc tgtgaacctg gt 632

```

&lt;210&gt; 82

&lt;211&gt; 1388

&lt;212&gt; DNA



&lt;213&gt; Homo sapiens

&lt;400&gt; 82

```

ctgctacgct tttttgacca agaactacag ttactcatgg aaatattacc ttacaattat 60
atthaaagat tcaactgtttg ctaatttaac atagcaatgt gaatgaaatt gccagaagtc 120
tgctttttta actgttgtac gcttcatgag tccaaatatg agattgtgac aatgtttatc 180
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cagctcaatg ctgtgaataa ctccctgact ccgcaatcaa ccaagggtcc cagccttttt 300
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tgtaagcaaa cttggatgca aaatatattg aataaaatca gatgcttgca tctgtagtga 1380
acataaaa

```

&lt;210&gt; 83

&lt;211&gt; 1015

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 83

```

atttggacac acaactccaa aattttcttc cacaacctct tgttaccttt tcagccaccc 60
gtgccccctt tcatcatacc tcttccacta ctagtacatg tataatactt ccyyccatggs 120
ccccwcgaac ccccgacctt tctttaccat catcacactg gaagactcca gtgggaacct 180
tctgggacgg gacagctttg aggttcgtgt ttgtgcctcc cctgggagag acccccgta 240
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&lt;210&gt; 84

&lt;211&gt; 969

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 84

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 tttttttttt tttaccctt tttatatatc aatttctat tttacaataa aattttgtta 960  
 tcacttaaa

&lt;210&gt; 85

&lt;211&gt; 3939

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 85

gaattcgggg ccgcaccgcg cgcaccgcgc catggggggc gcgtccggcc agcggggggc 60  
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acacctgagt ctgtgtccct tgtgggaagc cagggacagg accggctgct tgctgtctc 3900
ctgacagtc cagcaagacc ctttantggt tgcncannng 3939

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&lt;210&gt; 86

&lt;211&gt; 1470

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 86

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ttgaaccagc aggggtggccc acgcgtgct gagcctctg cgtgcgcggg gagccagctc 180
gtaactcgcc ggctgccact taccatgacc atgacccttc acaccaaagc ctccgggaatg 240
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tcggcgccgg tctacggcca gtcgggcac gcctacggcc ccgggtcgga ggcggccgc 480
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ccctactacc tggagaacga gccagcgcc tacgcccgtg gcgacacgg cctcccgcc 660
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aatgactatg cctctggcta ccattatggg gtctggctct gcgaaggctg caaggctttc 840
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tttgtcmeta acacttggat gaacacttca ttacaacatg cccatgtgtt ctgtcatcaa 1440

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1470

atgtcatata ttaaaagtac ttaatgctcg

&lt;210&gt; 87

&lt;211&gt; 1723

&lt;212&gt; DNA

&lt;213&gt; Mouse

&lt;400&gt; 87

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cgcactctaa attagagata gatttttttc tgatatacat ttcactctat tcaccacgag 120
cacaccacac gcacagtata cagttccacg aacggataca ttgcacaaga tgagatggcc 180
atgagcagcg tgaagaccac cagcgcgcag cgcagcgtca gccccagga ctttaaggcg 240
ccgtcgcctc catagcaggc ggggaagaag gcgcgactgc cttcctggaa gagagacttc 300
tccagcactt cgacggccgc gaagaagggc aacggatagg acagcagcgc cttggccacc 360
aggaagaggt tgaccacggc gcggatggag ccgggcaggt tatccgtgat gacttccttg 420
gtctcgtcgg cccaggtgag gtaggcgacg agcgcgaaga gacccttgag cacgcaggcg 480
gcgatgtgtg tccagttcat catgcagtgg aattcgtcgg gctgctgcat gttgccttcg 540
agagagggca ggaagatctg cgacgtgtag ctgaacacga tgatgccaat ggagatggga 600
aacttcttga cgtcgtatga gaacttcacc ttctcccagg cccaatcacg cgcgcgagag 660
agacagtaag cgtatgaccg gatgttgatg acgaagtggg ccagcgtaca cagcagactg 720
aacttggaac cggccttgag attcttcagg aaggcgcagg gcagcagcac cgctgtggct 780
atgatggacc aggacttctg cgacacgggc agccccggga aactgttgta catgaggttg 840
ccgctcacca cgacgtacaa gatacacgtc atcaccagct cgatgatctg cgccacattg 900
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cccagggcgc tctggctcat gaccctcgcg cctgacgttc gaggctggcc ccggtcacga 1680
cagtctggct cttggtggga ccggcccag aggcctcgtg ccg 1723

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&lt;210&gt; 88

&lt;211&gt; 401

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 88

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Met Pro Ile Met Gly Ser Ser Val Tyr Ile Thr Val Glu Leu Ala Ile
  1           5           10           15
Ala Val Leu Ala Ile Leu Gly Asn Val Leu Val Cys Trp Ala Val Trp
  20           25           30
Leu Asn Ser Asn Leu Gln Asn Val Thr Asn Tyr Phe Val Val Ser Leu
  35           40           45
Ala Ala Ala Asp Ile Ala Val Gly Val Leu Ala Ile Pro Phe Ala Ile
  50           55           60
Thr Ile Ser Thr Gly Phe Cys Ala Ala Cys His Gly Cys Leu Phe Ile
  65           70           75           80

```

Ala Cys Phe Val Leu Val Leu Thr Gln Ser Ser Ile Phe Ser Leu Leu  
85 90 95

Ala Ile Ala Ile Asp Arg Tyr Ile Ala Ile Arg Ile Pro Leu Arg Tyr  
100 105 110

Asn Gly Leu Val Thr Gly Thr Arg Ala Lys Gly Ile Ile Ala Ile Cys  
115 120 125

Trp Val Leu Ser Phe Ala Ile Gly Leu Thr Pro Met Leu Gly Trp Asn  
130 135 140

Asn Cys Gly Gln Pro Lys Glu Gly Lys Asn His Ser Gln Gly Cys Gly  
145 150 155 160

Glu Gly Gln Val Ala Cys Leu Phe Glu Asp Val Val Pro Met Asn Tyr  
165 170 175

Met Val Tyr Phe Asn Phe Phe Ala Cys Val Leu Val Pro Leu Leu Leu  
180 185 190

Met Leu Gly Val Tyr Leu Arg Ile Phe Leu Ala Ala Arg Arg Gln Leu  
195 200 205

Lys Gln Met Glu Ser Gln Pro Leu Pro Gly Glu Arg Ala Arg Ser Thr  
210 215 220

Leu Gln Lys Glu Val His Ala Ala Lys Ser Leu Ala Pro Leu His Ile  
225 230 235 240

Ile Asn Cys Phe Thr Phe Phe Cys Pro Asp Cys Ser His Ala Pro Leu  
245 250 255

Trp Leu Met Tyr Leu Ala Ile Val Leu Ser His Thr Asn Ser Val Val  
260 265 270

Asn Pro Phe Ile Tyr Ala Tyr Arg Ile Arg Glu Phe Arg Gln Thr Phe  
275 280 285

Arg Lys Ile Ile Arg Ser His Val Leu Arg Gln Gln Glu Pro Phe Lys  
290 295 300

Ala Ala Gly Thr Ser Ala Arg Val Leu Ala Ala His Gly Ser Asp Gly  
305 310 315 320

Glu Gln Val Ser Leu Arg Leu Asn Gly His Pro Pro Gly Val Trp Ala  
325 330 335

Asn Gly Ser Ala Pro His Pro Glu Arg Arg Pro Asn Gly Tyr Ala Leu  
340 345 350

Gly Leu Val Ser Gly Gly Ser Ala Gln Glu Ser Gln Gly Asn Thr Gly  
355 360 365

Leu Pro Asp Val Glu Leu Leu Ser His Glu Leu Lys Gly Val Cys Pro  
370 375 380

Glu Pro Pro Gly Leu Asp Asp Pro Leu Ala Gln Asp Gly Ala Gly Val  
385 390 395 400

Ser

<210> 89  
 <211> 682  
 <212> PRT  
 <213> Homo sapiens

<400> 89  
 Met Pro Arg Tyr Gly Ala Ser Leu Arg Gln Ser Cys Pro Arg Ser Gly  
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                   20                  25                  30  
 Met Gly Leu Val Leu Ala Leu Ala Leu Ala Leu Ala Leu Ala Leu Ser  
           35                  40                  45  
 Asp Ser Arg Val Leu Trp Ala Pro Ala Glu Ala His Pro Leu Ser Pro  
           50                  55                  60  
 Gln Gly His Pro Ala Arg Leu His Arg Ile Val Pro Arg Leu Arg Asp  
           65                  70                  75                  80  
 Val Phe Gly Trp Gly Asn Leu Thr Cys Pro Ile Cys Lys Gly Leu Phe  
                   85                  90                  95  
 Thr Ala Ile Asn Leu Gly Leu Lys Lys Glu Pro Asn Val Ala Arg Val  
                   100                  105                  110  
 Gly Ser Val Ala Ile Lys Leu Cys Asn Leu Leu Lys Ile Ala Pro Pro  
           115                  120                  125  
 Ala Val Cys Gln Ser Ile Val His Leu Phe Glu Asp Asp Met Val Glu  
           130                  135                  140  
 Val Trp Arg Arg Ser Val Leu Ser Pro Ser Glu Ala Cys Gly Leu Leu  
           145                  150                  155                  160  
 Leu Gly Ser Thr Cys Gly His Trp Asp Ile Phe Ser Ser Trp Asn Ile  
                   165                  170                  175  
 Ser Leu Pro Thr Val Pro Lys Pro Pro Pro Lys Pro Pro Ser Pro Pro  
           180                  185                  190  
 Ala Pro Gly Ala Pro Val Ser Arg Ile Leu Phe Leu Thr Asp Leu His  
           195                  200                  205  
 Trp Asp His Asp Tyr Leu Glu Gly Thr Asp Pro Asp Cys Ala Asp Pro  
           210                  215                  220  
 Leu Cys Cys Arg Arg Gly Ser Gly Leu Pro Pro Ala Ser Arg Pro Gly  
           225                  230                  235                  240  
 Ala Gly Tyr Trp Gly Glu Tyr Ser Lys Cys Asp Leu Pro Leu Arg Thr  
                   245                  250                  255  
 Leu Glu Ser Leu Leu Ser Gly Leu Gly Pro Ala Gly Pro Phe Asp Met  
           260                  265                  270  
 Val Tyr Trp Thr Gly Asp Ile Pro Ala His Asp Val Trp His Gln Thr

275	280	285
Arg Gln Asp Gln Leu Arg Ala Leu Thr Thr Val Thr Ala Leu Val Arg		
290	295	300
Lys Phe Leu Gly Pro Val Pro Val Tyr Pro Ala Val Gly Asn His Glu		
305	310	315
Ser Thr Pro Val Asn Ser Phe Pro Pro Pro Phe Ile Glu Gly Asn His		
325	330	335
Ser Ser Arg Trp Leu Tyr Glu Ala Met Ala Lys Ala Trp Glu Pro Trp		
340	345	350
Leu Pro Ala Glu Ala Leu Arg Thr Leu Arg Ile Gly Gly Phe Tyr Ala		
355	360	365
Leu Ser Pro Tyr Pro Gly Leu Arg Leu Ile Ser Leu Asn Met Asn Phe		
370	375	380
Cys Ser Arg Glu Asn Phe Trp Leu Leu Ile Asn Ser Thr Asp Pro Ala		
385	390	395
Gly Gln Leu Gln Trp Leu Val Gly Glu Leu Gln Ala Ala Glu Asp Arg		
405	410	415
Gly Asp Lys Val His Ile Ile Gly His Ile Pro Pro Gly His Cys Leu		
420	425	430
Lys Ser Trp Ser Trp Asn Tyr Tyr Arg Ile Val Ala Arg Tyr Glu Asn		
435	440	445
Thr Leu Ala Ala Gln Phe Phe Gly His Thr His Val Asp Glu Phe Glu		
450	455	460
Val Phe Tyr Asp Glu Glu Thr Leu Ser Arg Pro Leu Ala Val Ala Phe		
465	470	475
Leu Ala Pro Ser Ala Thr Thr Tyr Ile Gly Leu Asn Pro Leu Val Ser		
485	490	495
Glu Ala Glu Gly Ser Leu Pro Tyr Pro Gly Val Gly Gly Ile Gly Glu		
500	505	510
Gly Gly Trp Ser Gln Ser Leu Gln Ser Met Gly Arg Met Cys Gly Pro		
515	520	525
Ser Leu Glu Leu Pro Leu Leu Leu Ala Pro Pro Val Ser Pro Thr Ser		
530	535	540
Leu Ala Gly Tyr Arg Val Tyr Gln Ile Asp Gly Asn Tyr Ser Gly Ser		
545	550	555
Ser His Val Val Leu Asp His Glu Thr Tyr Ile Leu Asn Leu Thr Gln		
565	570	575
Ala Asn Ile Pro Gly Ala Ile Pro His Trp Gln Leu Leu Tyr Arg Ala		
580	585	590
Arg Glu Thr Tyr Gly Leu Pro Asn Thr Leu Pro Thr Ala Trp His Asn		
595	600	605

Leu Val Tyr Arg Met Arg Gly Asp Met Gln Leu Phe Gln Thr Phe Trp  
 610 615 620

Phe Leu Tyr His Lys Gly His Pro Pro Ser Glu Pro Cys Gly Thr Pro  
 625 630 635 640

Cys Arg Leu Ala Thr Leu Cys Ala Gln Leu Ser Ala Arg Ala Asp Ser  
 645 650 655

Pro Ala Leu Cys Arg His Leu Met Pro Asp Gly Ser Leu Pro Glu Ala  
 660 665 670

Gln Ser Leu Trp Pro Arg Pro Leu Phe Cys  
 675 680

<210> 90  
 <211> 515  
 <212> PRT  
 <213> Homo sapiens

<400> 90  
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Ile Pro Pro Trp Glu Ala Pro Lys Glu His Lys Tyr Lys Ala Glu Glu  
 20 25 30

His Thr Val Val Leu Thr Val Thr Gly Glu Pro Cys His Phe Pro Phe  
 35 40 45

Gln Tyr His Arg Gln Leu Tyr His Lys Cys Thr His Lys Gly Arg Pro  
 50 55 60

Gly Pro Gln Pro Trp Cys Ala Thr Thr Pro Asn Phe Asp Gln Asp Gln  
 65 70 75 80

Arg Trp Gly Tyr Cys Leu Glu Pro Lys Lys Val Lys Asp His Cys Ser  
 85 90 95

Lys His Ser Pro Cys Gln Lys Gly Gly Thr Cys Val Asn Met Pro Ser  
 100 105 110

Gly Pro His Cys Leu Cys Pro Gln His Leu Thr Gly Asn His Cys Gln  
 115 120 125

Lys Glu Lys Cys Phe Glu Pro Gln Leu Leu Arg Phe Phe His Lys Asn  
 130 135 140

Glu Ile Trp Tyr Arg Thr Glu Gln Ala Ala Val Ala Arg Cys Gln Cys  
 145 150 155 160

Lys Gly Pro Asp Ala His Cys Gln Arg Leu Ala Ser Gln Ala Cys Arg  
 165 170 175

Thr Asn Pro Cys Leu His Gly Gly Arg Cys Leu Glu Val Glu Gly His  
 180 185 190

Arg Leu Cys His Cys Pro Val Gly Tyr Thr Gly Pro Phe Cys Asp Val  
 195 200 205



Asp Thr Lys Ala Ser Cys Tyr Asp Gly Arg Gly Leu Ser Tyr Arg Gly  
 210 215 220  
 Leu Ala Arg Thr Thr Leu Ser Gly Ala Pro Cys Gln Pro Trp Ala Ser  
 225 230 235 240  
 Glu Ala Thr Tyr Arg Asn Val Thr Ala Glu Gln Ala Arg Asn Trp Gly  
 245 250 255  
 Leu Gly Gly His Ala Phe Cys Arg Asn Pro Asp Asn Asp Ile Arg Pro  
 260 265 270  
 Trp Cys Phe Val Leu Asn Arg Asp Arg Leu Ser Trp Glu Tyr Cys Asp  
 275 280 285  
 Leu Ala Gln Cys Gln Thr Pro Thr Gln Ala Ala Pro Pro Thr Pro Val  
 290 295 300  
 Ser Pro Arg Leu His Val Pro Leu Met Pro Ala Gln Pro Ala Pro Pro  
 305 310 315 320  
 Lys Pro Gln Pro Thr Thr Arg Thr Pro Pro Gln Ser Gln Thr Pro Gly  
 325 330 335  
 Ala Leu Pro Ala Lys Arg Glu Gln Pro Pro Ser Leu Thr Arg Asn Gly  
 340 345 350  
 Pro Leu Ser Cys Gly Gln Arg Leu Arg Lys Ser Leu Ser Ser Met Thr  
 355 360 365  
 Arg Val Val Gly Gly Leu Val Ala Leu Arg Gly Ala His Pro Tyr Ile  
 370 375 380  
 Ala Ala Leu Tyr Trp Gly His Ser Phe Cys Ala Gly Ser Leu Ile Ala  
 385 390 395 400  
 Pro Cys Trp Val Leu Thr Ala Ala His Cys Leu Gln Asp Arg Pro Ala  
 405 410 415  
 Pro Glu Asp Leu Thr Val Val Leu Gly Gln Glu Arg Arg Asn His Ser  
 420 425 430  
 Cys Glu Pro Cys Gln Thr Leu Ala Val Arg Ser Tyr Arg Leu His Glu  
 435 440 445  
 Ala Phe Ser Pro Val Ser Tyr Gln His Asp Leu Ala Leu Leu Arg Leu  
 450 455 460  
 Gln Glu Asp Ala Asp Gly Ser Cys Ala Leu Leu Ser Pro Tyr Val Gln  
 465 470 475 480  
 Pro Val Cys Leu Pro Ser Gly Ala Ala Arg Pro Ser Glu Thr Thr Leu  
 485 490 495  
 Cys Gln Val Ala Gly Trp Gly His Gln Phe Glu Ala Ser Leu Pro Met  
 500 505 510  
 Lys Leu Asn  
 515

<210> 91  
 <211> 775  
 <212> PRT  
 <213> Homo sapiens

<400> 91  
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 Leu Leu Leu Pro Gly Ser Leu Glu Glu Cys Gly His Ile Ser Val Ser  
                   20                  25                  30  
 Ala Pro Ile Val His Leu Gly Asp Pro Ile Thr Ala Ser Cys Ile Ile  
                   35                  40                  45  
 Lys Gln Asn Cys Ser His Leu Asp Pro Glu Pro Gln Ile Leu Trp Arg  
                   50                  55                  60  
 Leu Gly Ala Glu Leu Gln Pro Gly Gly Arg Gln Gln Arg Leu Ser Asp  
                   65                  70                  75                  80  
 Gly Thr Gln Glu Ser Ile Ile Thr Leu Pro His Leu Asn His Thr Gln  
                   85                  90                  95  
 Ala Phe Leu Ser Cys Cys Leu Asn Trp Gly Asn Ser Leu Gln Ile Leu  
                   100                  105                  110  
 Asp Gln Val Glu Leu Arg Ala Gly Tyr Pro Pro Ala Ile Pro His Asn  
                   115                  120                  125  
 Leu Ser Cys Leu Met Asn Leu Thr Thr Ser Ser Leu Ile Cys Gln Trp  
                   130                  135                  140  
 Glu Pro Gly Pro Glu Thr His Leu Pro Thr Ser Phe Thr Leu Lys Ser  
                   145                  150                  155                  160  
 Phe Lys Ser Arg Gly Asn Cys Gln Thr Gln Gly Asp Ser Ile Leu Asp  
                   165                  170                  175  
 Cys Val Pro Lys Asp Gly Gln Ser His Cys Cys Ile Pro Arg Lys His  
                   180                  185                  190  
 Leu Leu Leu Tyr Gln Asn Met Gly Ile Trp Val Gln Ala Glu Asn Ala  
                   195                  200                  205  
 Leu Gly Thr Ser Met Ser Pro Gln Leu Cys Leu Asp Pro Met Asp Val  
                   210                  215                  220  
 Val Lys Leu Glu Pro Pro Met Leu Arg Thr Met Asp Pro Ser Pro Glu  
                   225                  230                  235                  240  
 Ala Ala Pro Pro Gln Ala Gly Cys Leu Gln Leu Cys Trp Glu Pro Trp  
                   245                  250                  255  
 Gln Pro Gly Leu His Ile Asn Gln Lys Cys Glu Leu Arg His Lys Pro  
                   260                  265                  270  
 Gln Arg Gly Glu Ala Ser Trp Ala Leu Val Gly Pro Leu Pro Leu Glu  
                   275                  280                  285

Ala Leu Gln Tyr Glu Leu Cys Gly Leu Leu Pro Ala Thr Ala Tyr Thr  
 290 295 300

Leu Gln Ile Arg Cys Ile Arg Trp Pro Leu Pro Gly His Trp Ser Asp  
 305 310 315 320

Gly Ala Ile Leu Pro Leu Cys Asn Thr Thr Glu Leu Ser Cys Thr Phe  
 325 330 335

His Leu Pro Ser Glu Ala Gln Glu Val Ala Leu Val Ala Tyr Asn Ser  
 340 345 350

Ala Gly Thr Ser Arg Pro Thr Pro Val Val Phe Ser Glu Ser Arg Gly  
 355 360 365

Pro Ala Leu Thr Arg Leu His Ala Met Ala Arg Asp Pro His Ser Leu  
 370 375 380

Trp Val Gly Trp Glu Pro Pro Asn Pro Trp Pro Gln Gly Tyr Val Ile  
 385 390 395 400

Glu Trp Gly Leu Gly Pro Pro Ser Ala Ser Asn Ser Asn Lys Thr Trp  
 405 410 415

Arg Met Glu Gln Asn Gly Arg Ala Thr Gly Phe Leu Leu Lys Glu Asn  
 420 425 430

Ile Arg Pro Phe Gln Leu Tyr Glu Ile Ile Val Thr Pro Leu Tyr Gln  
 435 440 445

Asp Thr Met Gly Pro Ser Gln His Val Tyr Ala Tyr Ser Gln Glu Met  
 450 455 460

Ala Pro Ser His Ala Pro Glu Leu His Leu Lys His Ile Gly Lys Thr  
 465 470 475 480

Trp Ala Gln Leu Glu Trp Val Pro Glu Pro Pro Glu Leu Gly Lys Ser  
 485 490 495

Pro Leu Thr His Tyr Thr Ile Phe Trp Thr Asn Ala Gln Asn Gln Ser  
 500 505 510

Phe Ser Ala Ile Leu Asn Ala Ser Ser Arg Gly Phe Val Leu His Gly  
 515 520 525

Leu Glu Pro Ala Ser Leu Tyr His Ile His Leu Met Ala Ala Ser Gln  
 530 535 540

Ala Gly Ala Thr Asn Ser Thr Val Leu Thr Leu Met Thr Leu Thr Pro  
 545 550 555 560

Glu Gly Ser Glu Leu His Ile Ile Leu Gly Leu Phe Gly Leu Leu Leu  
 565 570 575

Leu Leu Thr Cys Leu Cys Gly Thr Ala Trp Leu Cys Cys Ser Pro Asn  
 580 585 590

Arg Lys Asn Pro Leu Trp Pro Ser Val Pro Asp Pro Ala His Ser Ser  
 595 600 605

Leu Gly Ser Trp Val Pro Thr Ile Met Glu Glu Asp Ala Phe Gln Leu

610                      615                      620  
 Pro Gly Leu Gly Thr Pro Pro Ile Thr Lys Leu Thr Val Leu Glu Glu  
 625                      630                      635                      640  
 Asp Glu Lys Lys Pro Val Pro Trp Glu Ser His Asn Ser Ser Glu Thr  
                     645                      650                      655  
 Cys Gly Leu Pro Thr Leu Val Gln Thr Tyr Val Leu Gln Gly Asp Pro  
                     660                      665                      670  
 Arg Ala Val Ser Thr Gln Pro Gln Ser Gln Ser Gly Thr Ser Asp Gln  
                     675                      680                      685  
 Val Leu Tyr Gly Gln Leu Leu Gly Ser Pro Thr Ser Pro Gly Pro Gly  
                     690                      695                      700  
 His Tyr Leu Arg Cys Asp Ser Thr Gln Pro Leu Leu Ala Gly Leu Thr  
 705                      710                      715                      720  
 Pro Ser Pro Lys Ser Tyr Glu Asn Leu Trp Phe Gln Ala Ser Pro Leu  
                     725                      730                      735  
 Gly Thr Leu Val Thr Pro Ala Pro Ser Gln Glu Asp Asp Cys Val Phe  
                     740                      745                      750  
 Gly Pro Leu Leu Asn Phe Pro Leu Leu Gln Gly Ile Arg Val His Gly  
                     755                      760                      765  
 Met Glu Ala Leu Gly Ser Phe  
                     770                      775  
  
 <210> 92  
 <211> 873  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 92  
 Met Ala Arg Leu Gly Asn Cys Ser Leu Thr Trp Ala Ala Leu Ile Ile  
   1                      5                      10                      15  
 Leu Leu Leu Pro Gly Ser Leu Glu Glu Cys Gly His Ile Ser Val Ser  
                     20                      25                      30  
 Ala Pro Ile Val His Leu Gly Asp Pro Ile Thr Ala Ser Cys Ile Ile  
                     35                      40                      45  
 Lys Gln Asn Cys Ser His Leu Asp Pro Glu Pro Gln Ile Leu Trp Arg  
                     50                      55                      60  
 Leu Gly Ala Glu Leu Gln Pro Gly Gly Arg Gln Gln Arg Leu Ser Asp  
                     65                      70                      75                      80  
 Gly Thr Gln Glu Ser Ile Ile Thr Leu Pro His Leu Asn His Thr Gln  
                     85                      90                      95  
 Ala Phe Leu Ser Cys Cys Leu Asn Trp Gly Asn Ser Leu Gln Ile Leu  
                     100                      105                      110  
 Asp Gln Val Glu Leu Arg Ala Gly Tyr Pro Pro Ala Ile Pro His Asn

115	120	125
Leu Ser Cys Leu Met Asn	Leu Thr Thr Ser Ser	Leu Ile Cys Gln Trp
130	135	140
Glu Pro Gly Pro Glu Thr His	Leu Pro Thr Ser Phe Thr	Leu Lys Ser
145	150	155
Phe Lys Ser Arg Gly Asn Cys	Gln Thr Gln Gly Asp Ser	Ile Leu Asp
165	170	175
Cys Val Pro Lys Asp Gly Gln Ser	His Cys Cys Ile Pro Arg	Lys His
180	185	190
Leu Leu Leu Tyr Gln Asn Met	Gly Ile Trp Val Gln Ala	Glu Asn Ala
195	200	205
Leu Gly Thr Ser Met Ser Pro	Gln Leu Cys Leu Asp Pro	Met Asp Val
210	215	220
Val Lys Leu Glu Pro Pro Met	Leu Arg Thr Met Asp Pro	Ser Pro Glu
225	230	235
Ala Ala Pro Pro Gln Ala Gly	Cys Leu Gln Leu Cys Trp	Glu Pro Trp
245	250	255
Gln Pro Gly Leu His Ile Asn	Gln Lys Cys Glu Leu Arg	His Lys Pro
260	265	270
Gln Arg Gly Glu Ala Ser Trp	Ala Leu Val Gly Pro Leu	Pro Leu Glu
275	280	285
Ala Leu Gln Tyr Glu Leu Cys	Gly Leu Leu Pro Ala Thr	Ala Tyr Thr
290	295	300
Leu Gln Ile Arg Cys Ile Arg	Trp Pro Leu Pro Gly His	Trp Ser Asp
305	310	315
Trp Ser Pro Ser Leu Glu Leu	Arg Thr Thr Glu Arg Ala	Pro Thr Val
325	330	335
Arg Leu Asp Thr Trp Trp Arg	Gln Arg Gln Leu Asp Pro	Arg Thr Val
340	345	350
Gln Leu Phe Trp Lys Pro Val	Pro Leu Glu Glu Asp Ser	Gly Arg Ile
355	360	365
Gln Gly Tyr Val Val Ser Trp	Arg Pro Ser Gly Gln Ala	Gly Ala Ile
370	375	380
Leu Pro Leu Cys Asn Thr Thr	Glu Leu Ser Cys Thr Phe	His Leu Pro
385	390	395
Ser Glu Ala Gln Glu Val Ala	Leu Val Ala Tyr Asn Ser	Ala Gly Thr
405	410	415
Ser Arg Pro Thr Pro Val Val	Phe Ser Glu Ser Arg Gly	Pro Ala Leu
420	425	430
Thr Arg Leu His Ala Met Ala	Arg Asp Pro His Ser Leu	Trp Val Gly
435	440	445

Trp Glu Pro Pro Asn Pro Trp Pro Gln Gly Tyr Val Ile Glu Trp Gly  
 450 455 460

Leu Gly Pro Pro Ser Ala Ser Asn Ser Asn Lys Thr Trp Arg Met Glu  
 465 470 475 480

Gln Asn Gly Arg Ala Thr Gly Phe Leu Leu Lys Glu Asn Ile Arg Pro  
 485 490 495

Phe Gln Leu Tyr Glu Ile Ile Val Thr Pro Leu Tyr Gln Asp Thr Met  
 500 505 510

Gly Pro Ser Gln His Val Tyr Ala Tyr Ser Gln Glu Met Ala Pro Ser  
 515 520 525

His Ala Pro Glu Leu His Leu Lys His Ile Gly Lys Thr Trp Ala Gln  
 530 535 540

Leu Glu Trp Val Pro Glu Pro Pro Glu Leu Gly Lys Ser Pro Leu Thr  
 545 550 555 560

His Tyr Thr Ile Phe Trp Thr Asn Ala Gln Asn Gln Ser Phe Cys Glu  
 565 570 575

Ser Xaa Leu Ser Ser Pro Thr Ala Pro Glu Gly Leu Glu Gly Gly Ala  
 580 585 590

Gln Leu Pro Arg Arg Xaa Phe Thr Ile Gln Ala Tyr Ala Asp Arg Thr  
 595 600 605

Pro Leu Pro Ala Ala Ile Leu Asn Ala Ser Ser Arg Gly Phe Val Leu  
 610 615 620

His Gly Leu Glu Pro Ala Ser Leu Tyr His Ile His Leu Met Ala Ala  
 625 630 635 640

Ser Gln Ala Gly Ala Thr Asn Ser Thr Val Leu Thr Leu Met Thr Leu  
 645 650 655

Thr Pro Glu Gly Ser Glu Leu His Ile Ile Leu Gly Leu Phe Gly Leu  
 660 665 670

Leu Leu Leu Leu Thr Cys Leu Cys Gly Thr Ala Trp Leu Cys Cys Ser  
 675 680 685

Pro Asn Arg Lys Asn Pro Leu Trp Pro Ser Val Pro Asp Pro Ala His  
 690 695 700

Ser Ser Leu Gly Ser Trp Val Pro Thr Ile Met Glu Glu Asp Ala Phe  
 705 710 715 720

Gln Leu Pro Gly Leu Gly Thr Pro Pro Ile Thr Lys Leu Thr Val Leu  
 725 730 735

Glu Glu Asp Glu Lys Lys Pro Val Pro Trp Glu Ser His Asn Ser Ser  
 740 745 750

Glu Thr Cys Gly Leu Pro Thr Leu Val Gln Thr Tyr Val Leu Gln Gly  
 755 760 765

Asp Pro Arg Ala Val Ser Thr Gln Pro Gln Ser Gln Ser Gly Thr Ser  
770 775 780

Asp Gln Val Leu Tyr Gly Gln Leu Leu Gly Ser Pro Thr Ser Pro Gly  
785 790 795 800

Pro Gly His Tyr Leu Arg Cys Asp Ser Thr Gln Pro Leu Leu Ala Gly  
805 810 815

Leu Thr Pro Ser Pro Lys Ser Tyr Glu Asn Leu Trp Phe Gln Ala Ser  
820 825 830

Pro Leu Gly Thr Leu Val Thr Pro Ala Pro Ser Gln Glu Asp Asp Cys  
835 840 845

Val Phe Gly Pro Leu Leu Asn Phe Pro Leu Leu Gln Gly Ile Arg Val  
850 855 860

His Gly Met Glu Ala Leu Gly Ser Phe  
865 870

<210> 93

<211> 837

<212> PRT

<213> Homo sapiens

<400> 93

Met Gln Lys Ile Met His Ile Ser Val Leu Leu Ser Pro Val Leu Trp  
1 5 10 15

Gly Leu Ile Phe Gly Val Ser Ser Asn Ser Ile Gln Ile Gly Gly Leu  
20 25 30

Phe Pro Arg Gly Ala Asp Gln Glu Tyr Ser Ala Phe Arg Val Gly Met  
35 40 45

Val Gln Phe Ser Thr Ser Glu Phe Arg Leu Thr Pro His Ile Asp Asn  
50 55 60

Leu Glu Val Ala Asn Ser Phe Ala Val Thr Asn Ala Phe Cys Ser Gln  
65 70 75 80

Phe Ser Arg Gly Val Tyr Ala Ile Phe Gly Phe Tyr Asp Lys Lys Ser  
85 90 95

Val Asn Thr Ile Thr Ser Phe Cys Gly Thr Leu His Val Ser Phe Ile  
100 105 110

Thr Pro Ser Phe Pro Thr Asp Gly Thr His Pro Phe Val Ile Gln Met  
115 120 125

Arg Pro Asp Leu Lys Gly Ala Leu Leu Ser Leu Ile Glu Tyr Tyr Gln  
130 135 140

Trp Asp Lys Phe Ala Tyr Leu Tyr Asp Ser Asp Arg Gly Leu Ser Thr  
145 150 155 160

Leu Gln Ala Val Leu Asp Ser Ala Ala Glu Lys Lys Trp Gln Val Thr  
165 170 175

Ala Ile Asn Val Gly Asn Ile Asn Asn Asp Lys Lys Asp Glu Met Tyr  
 180 185 190  
 Arg Ser Leu Phe Gln Asp Leu Glu Leu Lys Lys Glu Arg Arg Val Ile  
 195 200 205  
 Leu Asp Cys Glu Arg Asp Lys Val Asn Asp Ile Val Asp Gln Val Ile  
 210 215 220  
 Thr Ile Gly Lys His Val Lys Gly Tyr His Tyr Ile Ile Ala Asn Leu  
 225 230 235 240  
 Glu Phe Thr Asp Gly Asp Leu Leu Lys Ile Gln Phe Gly Gly Ala Asn  
 245 250 255  
 Val Ser Gly Phe Gln Ile Val Asp Tyr Asp Asp Ser Leu Val Ser Lys  
 260 265 270  
 Phe Ile Glu Arg Trp Ser Thr Leu Glu Glu Lys Glu Tyr Pro Gly Ala  
 275 280 285  
 His Thr Thr Thr Ile Lys Tyr Thr Ser Ala Leu Thr Tyr Asp Ala Val  
 290 295 300  
 Gln Val Met Thr Glu Ala Phe Arg Asn Leu Arg Lys Gln Arg Ile Glu  
 305 310 315 320  
 Ile Ser Arg Arg Gly Asn Ala Gly Asp Cys Leu Ala Asn Pro Ala Val  
 325 330 335  
 Pro Trp Gly Gln Gly Val Glu Ile Glu Arg Ala Leu Lys Gln Val Gln  
 340 345 350  
 Val Glu Gly Leu Ser Gly Asn Ile Lys Phe Asp Gln Asn Gly Lys Arg  
 355 360 365  
 Ile Asn Tyr Thr Ile Asn Ile Met Glu Leu Lys Thr Asn Gly Pro Arg  
 370 375 380  
 Lys Ile Gly Tyr Trp Ser Glu Val Asp Lys Met Val Val Thr Leu Thr  
 385 390 395 400  
 Glu Leu Pro Ser Gly Asn Asp Thr Ser Gly Leu Glu Asn Lys Thr Val  
 405 410 415  
 Val Val Thr Thr Ile Leu Glu Ser Pro Tyr Val Met Met Lys Lys Asn  
 420 425 430  
 His Glu Met Leu Glu Gly Asn Glu Arg Tyr Glu Gly Tyr Cys Val Asp  
 435 440 445  
 Leu Ala Ala Glu Ile Ala Lys His Cys Gly Phe Lys Tyr Lys Leu Thr  
 450 455 460  
 Ile Val Gly Asp Gly Lys Tyr Gly Ala Arg Asp Ala Asp Thr Lys Ile  
 465 470 475 480  
 Trp Asn Gly Met Val Gly Glu Leu Val Tyr Gly Lys Ala Asp Ile Ala  
 485 490 495  
 Ile Ala Pro Leu Thr Ile Thr Leu Val Arg Glu Glu Val Ile Asp Phe



500	505	510
Ser Lys Pro Phe Met Ser Leu Gly Ile Ser Ile Met Ile Lys Lys Pro 515	520	525
Gln Lys Ser Lys Pro Gly Val Phe Ser Phe Leu Asp Pro Leu Ala Tyr 530	535	540
Glu Ile Trp Met Cys Ile Val Phe Ala Tyr Ile Gly Val Ser Val Val 545	550	555 560
Leu Phe Leu Val Ser Arg Phe Ser Pro Tyr Glu Trp His Thr Glu Glu 565	570	575
Phe Glu Asp Gly Arg Glu Thr Gln Ser Ser Glu Ser Thr Asn Glu Phe 580	585	590
Gly Ile Phe Asn Ser Leu Trp Phe Ser Leu Gly Ala Phe Met Arg Gln 595	600	605
Gly Cys Asp Ile Ser Pro Arg Ser Leu Ser Gly Arg Ile Val Gly Gly 610	615	620
Val Trp Trp Phe Phe Thr Leu Ile Ile Ile Ser Ser Tyr Thr Ala Asn 625	630	635 640
Leu Ala Ala Phe Leu Thr Val Glu Arg Met Val Ser Pro Ile Glu Ser 645	650	655
Ala Glu Asp Leu Ser Lys Gln Thr Glu Ile Ala Tyr Gly Thr Leu Asp 660	665	670
Ser Gly Ser Thr Lys Glu Phe Phe Arg Arg Ser Lys Ile Ala Val Phe 675	680	685
Asp Lys Met Trp Thr Tyr Met Arg Ser Ala Glu Pro Ser Val Phe Val 690	695	700
Arg Thr Thr Ala Glu Gly Val Ala Arg Val Arg Lys Ser Lys Gly Lys 705	710	715 720
Tyr Ala Tyr Leu Leu Glu Ser Thr Met Asn Glu Tyr Ile Glu Gln Arg 725	730	735
Lys Pro Cys Asp Thr Met Lys Val Gly Gly Asn Leu Asp Ser Lys Gly 740	745	750
Tyr Gly Ile Ala Thr Pro Lys Gly Ser Ser Leu Gly Thr Pro Val Asn 755	760	765
Leu Ala Val Leu Lys Leu Ser Glu Gln Gly Val Leu Asp Lys Leu Lys 770	775	780
Asn Lys Trp Trp Tyr Asp Lys Gly Glu Xaa Gly Xaa Gly Glu Val Ile 785	790	795 800
Pro Arg Ser Ala Pro Val Arg Lys Val Met Gly Asn Ser Met Gln Asn 805	810	815
Lys Val Ser Ser Ser Tyr Ala Gln Cys Gly His Ser Val His Pro Ser 820	825	830

Phe Gln Arg Leu Ser  
835

<210> 94  
<211> 156  
<212> PRT  
<213> Homo sapiens

<400> 94  
Met Lys Ser Ile Tyr Phe Val Ala Gly Leu Phe Val Met Leu Val Gln  
1 5 10 15  
Gly Ser Trp Gln Arg Ser Leu Gln Asp Thr Glu Glu Lys Ser Arg Ser  
20 25 30  
Phe Ser Ala Ser Gln Ala Asp Pro Leu Ser Asp Pro Asp Gln Met Asn  
35 40 45  
Glu Asp Lys Arg His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys  
50 55 60  
Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn  
65 70 75 80  
Thr Lys Arg Asn Arg Asn Asn Ile Ala Lys Arg His Asp Glu Phe Glu  
85 90 95  
Arg His Ala Glu Gly Thr Phe Thr Ser Val Ile Phe Pro Glu Glu Val  
100 105 110  
Ala Ile Val Glu Glu Leu Gly Arg Arg His Ala Asp Gly Ser Phe Ser  
115 120 125  
Asp Glu Met Asn Thr Ile Ser Asp Asn Leu Ala Ala Arg Asp Phe Ile  
130 135 140  
Asn Trp Leu Ile Gln Thr Lys Ile Thr Asp Arg Lys  
145 150 155

<210> 95  
<211> 303  
<212> PRT  
<213> Homo sapiens

<400> 95  
Met Leu Ser Phe Ile Ser Gly Thr Ala Arg Lys Thr Leu His Phe Glu  
1 5 10 15  
Ile Ser Lys Glu Gly Ser Asp Leu Ser Val Val Glu Arg Ala Glu Val  
20 25 30  
Trp Leu Phe Leu Lys Val Pro Lys Ala Asn Arg Thr Arg Thr Lys Val  
35 40 45  
Thr Ile Arg Leu Phe Gln Gln Gln Lys His Pro Gln Gly Ser Leu Asp  
50 55 60  
Thr Gly Glu Glu Ala Glu Glu Val Gly Leu Lys Gly Glu Arg Ser Glu

65 70 75 80

Leu Leu Leu Ser Glu Lys Val Val Asp Ala Arg Lys Ser Thr Trp His  
85 90 95

Val Phe Pro Val Ser Ser Ser Ile Gln Arg Leu Leu Asp Gln Gly Lys  
100 105 110

Ser Ser Leu Asp Val Arg Ile Ala Cys Glu Gln Cys Gln Glu Ser Gly  
115 120 125

Ala Ser Leu Val Leu Leu Gly Lys Lys Lys Lys Lys Glu Glu Glu Gly  
130 135 140

Glu Gly Lys Lys Lys Gly Gly Gly Glu Gly Gly Ala Gly Ala Asp Glu  
145 150 155 160

Glu Lys Glu Gln Ser His Arg Pro Phe Leu Met Leu Gln Ala Arg Gln  
165 170 175

Ser Glu Asp His Pro His Arg Arg Arg Arg Arg Gly Leu Glu Cys Asp  
180 185 190

Gly Lys Val Asn Ile Cys Cys Lys Lys Gln Phe Phe Val Ser Phe Lys  
195 200 205

Asp Ile Gly Trp Asn Asp Trp Ile Ile Ala Pro Ser Gly Tyr His Ala  
210 215 220

Asn Tyr Cys Glu Gly Glu Cys Pro Ser His Ile Ala Gly Thr Ser Gly  
225 230 235 240

Ser Ser Leu Ser Phe His Ser Thr Val Ile Asn His Tyr Arg Met Arg  
245 250 255

Gly His Ser Pro Phe Ala Asn Leu Lys Ser Cys Cys Val Pro Thr Lys  
260 265 270

Leu Arg Pro Met Ser Met Leu Tyr Tyr Asp Asp Gly Gln Asn Ile Ile  
275 280 285

Lys Lys Asp Ile Gln Asn Met Ile Val Glu Glu Cys Gly Cys Ser  
290 295 300

<210> 96  
<211> 194  
<212> PRT  
<213> Homo sapiens

<400> 96  
Met Asn Ser Phe Ser Thr Ser Ala Phe Gly Pro Val Ala Phe Ser Leu  
1 5 10 15  
Gly Leu Leu Leu Val Leu Pro Ala Ala Phe Pro Ala Pro Val Pro Pro  
20 25 30  
Gly Glu Asp Ser Lys Asp Val Ala Ala Pro His Arg Gln Pro Leu Thr  
35 40 45  
Ser Ser Glu Arg Ile Asp Lys Gln Ile Arg Tyr Ile Leu Asp Gly Ile

50

55

60

Ser Ala Leu Arg Lys Glu Thr Cys Asn Xaa Ser Asn Met Cys Glu Lys  
65 70 75 80

Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu Val Lys  
85 90 95

Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr Leu Gln  
100 105 110

Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln Met Ser  
115 120 125

Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn Leu Asp  
130 135 140

Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu Thr Lys  
145 150 155 160

Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His Leu Ile  
165 170 175

Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala Leu Arg  
180 185 190

Gln Met

<210> 97

<211> 148

<212> PRT

<213> Homo sapiens

<400> 97

Met Asn Ser Phe Ser Thr Thr Cys Asn Lys Ser Asn Met Cys Glu Ser  
1 5 10 15

Ser Lys Glu Ala Leu Ala Glu Asn Asn Leu Asn Leu Pro Lys Met Ala  
20 25 30

Glu Lys Asp Gly Cys Phe Gln Ser Gly Phe Asn Glu Glu Thr Cys Leu  
35 40 45

Val Lys Ile Ile Thr Gly Leu Leu Glu Phe Glu Val Tyr Leu Glu Tyr  
50 55 60

Leu Gln Asn Arg Phe Glu Ser Ser Glu Glu Gln Ala Arg Ala Val Gln  
65 70 75 80

Met Ser Thr Lys Val Leu Ile Gln Phe Leu Gln Lys Lys Ala Lys Asn  
85 90 95

Leu Asp Ala Ile Thr Thr Pro Asp Pro Thr Thr Asn Ala Ser Leu Leu  
100 105 110

Thr Lys Leu Gln Ala Gln Asn Gln Trp Leu Gln Asp Met Thr Thr His  
115 120 125

Leu Ile Leu Arg Ser Phe Lys Glu Phe Leu Gln Ser Ser Leu Arg Ala

130

135

140

Leu Arg Gln Met  
145

<210> 98  
<211> 220  
<212> PRT  
<213> Homo sapiens

<400> 98  
Met Pro Arg Leu Phe Leu Phe His Leu Leu Glu Phe Cys Leu Leu Leu  
1 5 10 15  
Asn Gln Phe Ser Arg Ala Val Ala Ala Lys Trp Lys Asp Asp Val Ile  
20 25 30  
Lys Leu Cys Gly Arg Glu Leu Val Arg Ala Gln Ile Ala Ile Cys Gly  
35 40 45  
Met Ser Thr Trp Ser Lys Arg Ser Leu Ser Gln Glu Asp Ala Pro Gln  
50 55 60  
Thr Pro Arg Pro Val Ala Ala Gly Asp Phe Ile Gln Thr Val Ser Leu  
65 70 75 80  
Gly Ile Ser Pro Asp Gly Gly Lys Ala Leu Arg Thr Gly Ser Cys Phe  
85 90 95  
Thr Arg Glu Phe Leu Gly Ala Leu Ser Lys Leu Val Pro Ser Phe Ile  
100 105 110  
Asn Lys Asp Thr Glu Thr Ile Ile Ile Met Leu Glu Phe Ile Ala Asn  
115 120 125  
Leu Pro Pro Glu Leu Lys Ala Ala Leu Ser Glu Arg Gln Pro Ser Leu  
130 135 140  
Pro Glu Leu Gln Gln Tyr Val Pro Xaa Leu Lys Asp Ser Ser Leu Leu  
145 150 155 160  
Phe Glu Glu Phe Lys Lys Leu Ile Arg Asn Arg Gln Ser Glu Ala Ala  
165 170 175  
Asp Ser Asn Pro Ser Glu Leu Lys Tyr Leu Gly Leu Asp Thr His Ser  
180 185 190  
Gln Lys Lys Arg Arg Pro Tyr Val Ala Leu Phe Glu Lys Cys Cys Leu  
195 200 205  
Ile Gly Cys Thr Lys Arg Ser Leu Ala Lys Tyr Cys  
210 215 220

<210> 99  
<211> 87  
<212> PRT  
<213> Homo sapiens

<400> 99

Met Lys Leu Cys Val Thr Val Leu Ser Leu Leu Met Leu Val Ala Ala  
 1 5 10 15  
 Phe Cys Ser Pro Ala Leu Ser Ala Pro Met Gly Ser Asp Pro Pro Thr  
 20 25 30  
 Ala Cys Cys Phe Ser Tyr Thr Ala Arg Lys Leu Pro Arg Asn Phe Val  
 35 40 45  
 Val Asp Tyr Tyr Glu Thr Ser Ser Leu Cys Ser Gln Pro Ala Val Val  
 50 55 60  
 Gly Lys Gln Val Cys Ala Asp Pro Ser Glu Ser Trp Val Gln Glu Tyr  
 65 70 75 80  
 Val Tyr Asp Leu Glu Leu Asn  
 85

<210> 100  
 <211> 731  
 <212> PRT  
 <213> Homo sapiens

<400> 100

Met Gly Leu Ala Trp Gly Leu Gly Val Leu Phe Leu Met His Val Cys  
 1 5 10 15  
 Gly Thr Asn Arg Ile Pro Glu Ser Gly Gly Asp Asn Ser Val Phe Asp  
 20 25 30  
 Ile Phe Glu Leu Thr Gly Ala Ala Arg Lys Gly Ser Gly Arg Arg Leu  
 35 40 45  
 Val Lys Gly Pro Asp Pro Ser Ser Pro Ala Phe Arg Ile Glu Asp Ala  
 50 55 60  
 Asn Leu Ile Pro Pro Val Pro Asp Asp Lys Phe Gln Asp Leu Val Asp  
 65 70 75 80  
 Ala Val Arg Ala Glu Lys Gly Phe Leu Leu Leu Ala Ser Leu Arg Gln  
 85 90 95  
 Met Lys Lys Thr Arg Gly Thr Leu Leu Ala Leu Glu Arg Lys Asp His  
 100 105 110  
 Ser Gly Gln Val Phe Ser Val Val Ser Asn Gly Lys Ala Gly Thr Leu  
 115 120 125  
 Asp Leu Ser Leu Thr Val Gln Gly Lys Gln His Val Val Ser Val Glu  
 130 135 140  
 Glu Ala Leu Leu Ala Thr Gly Gln Trp Lys Ser Ile Thr Leu Phe Val  
 145 150 155 160  
 Gln Glu Asp Arg Ala Gln Leu Tyr Ile Asp Cys Glu Lys Met Glu Asn  
 165 170 175  
 Ala Glu Leu Asp Val Pro Ile Gln Ser Val Phe Thr Arg Asp Leu Ala  
 180 185 190

Ser Ile Ala Arg Leu Arg Ile Ala Lys Gly Gly Val Asn Asp Asn Phe  
 195 200 205  
 Gln Gly Val Leu Gln Asn Val Arg Phe Val Phe Gly Thr Thr Pro Glu  
 210 215 220  
 Asp Ile Leu Arg Asn Lys Gly Cys Ser Ser Ser Thr Ser Val Leu Leu  
 225 230 235 240  
 Thr Leu Asp Asn Asn Val Val Asn Gly Ser Ser Pro Ala Ile Arg Thr  
 245 250 255  
 Asn Tyr Ile Gly His Lys Thr Lys Asp Leu Gln Ala Ile Cys Gly Ile  
 260 265 270  
 Ser Cys Asp Glu Leu Ser Ser Met Val Leu Glu Leu Arg Gly Leu Arg  
 275 280 285  
 Thr Ile Val Thr Thr Leu Gln Asp Ser Ile Arg Lys Val Thr Glu Glu  
 290 295 300  
 Asn Lys Glu Leu Ala Asn Glu Leu Arg Arg Pro Pro Leu Cys Tyr His  
 305 310 315 320  
 Asn Gly Val Gln Tyr Arg Asn Asn Glu Glu Trp Thr Val Asp Ser Cys  
 325 330 335  
 Thr Glu Cys His Cys Gln Asn Ser Val Thr Ile Cys Lys Lys Val Ser  
 340 345 350  
 Cys Pro Ile Met Pro Cys Ser Asn Ala Thr Val Pro Asp Gly Glu Cys  
 355 360 365  
 Cys Pro Arg Cys Trp Pro Ser Asp Ser Ala Asp Asp Gly Trp Ser Pro  
 370 375 380  
 Trp Ser Glu Trp Thr Ser Cys Ser Thr Ser Cys Gly Asn Gly Ile Gln  
 385 390 395 400  
 Gln Arg Gly Arg Ser Cys Asp Ser Leu Asn Asn Arg Cys Glu Gly Ser  
 405 410 415  
 Ser Val Gln Thr Arg Thr Cys His Ile Gln Glu Cys Asp Lys Arg Phe  
 420 425 430  
 Lys Gln Asp Gly Gly Trp Ser His Trp Ser Pro Trp Ser Ser Cys Ser  
 435 440 445  
 Val Thr Cys Gly Asp Gly Val Ile Thr Arg Ile Arg Leu Cys Asn Ser  
 450 455 460  
 Pro Ser Pro Gln Met Asn Gly Lys Pro Cys Glu Gly Glu Ala Arg Glu  
 465 470 475 480  
 Thr Lys Ala Cys Lys Lys Asp Ala Cys Pro Ile Asn Gly Gly Trp Gly  
 485 490 495  
 Pro Trp Ser Pro Trp Asp Ile Cys Ser Val Thr Cys Gly Gly Gly Val  
 500 505 510  
 Gln Lys Arg Ser Arg Leu Cys Asn Asn Pro Thr Pro Gln Phe Gly Gly

515                                      520                                      525  
 Lys Asp Cys Val Gly Asp Val Thr Glu Asn Gln Ile Cys Asn Lys Gln  
 530                                      535                                      540  
 Asp Cys Pro Ile Asp Gly Cys Leu Ser Asn Pro Cys Phe Ala Gly Val  
 545                                      550                                      555                                      560  
 Lys Cys Thr Ser Tyr Pro Asp Gly Ser Trp Lys Cys Gly Ala Cys Pro  
 565                                      570                                      575  
 Pro Gly Tyr Ser Gly Asn Gly Ile Gln Cys Thr Asp Val Asp Glu Cys  
 580                                      585                                      590  
 Lys Glu Val Pro Asp Ala Cys Phe Asn His Asn Gly Glu His Arg Cys  
 595                                      600                                      605  
 Glu Asn Thr Asp Pro Gly Tyr Asn Cys Leu Pro Cys Pro Pro Arg Phe  
 610                                      615                                      620  
 Thr Gly Ser Gln Pro Phe Gly Gln Gly Val Glu His Ala Thr Ala Asn  
 625                                      630                                      635                                      640  
 Lys Gln Val Cys Lys Pro Arg Asn Pro Cys Thr Asp Gly Thr His Asp  
 645                                      650                                      655  
 Cys Asn Lys Asn Ala Lys Cys Asn Tyr Leu Gly His Tyr Ser Asp Pro  
 660                                      665                                      670  
 Met Tyr Arg Cys Glu Cys Lys Pro Gly Tyr Ala Gly Asn Gly Ile Ile  
 675                                      680                                      685  
 Cys Gly Glu Asp Thr Asp Leu Asp Gly Trp Pro Asn Glu Asn Leu Val  
 690                                      695                                      700  
 Cys Val Ala Asn Ala Thr Tyr His Cys Lys Lys Asp Asn Cys Pro Asn  
 705                                      710                                      715                                      720  
 Leu Pro Gln Asp Pro Ala Pro Cys Pro Arg Ser  
 725                                      730

<210> 101  
 <211> 555  
 <212> PRT  
 <213> Homo sapiens

<400> 101  
 Met Gly Leu Ala Trp Gly Leu Gly Val Leu Phe Leu Met His Val Cys  
 1                                      5                                      10                                      15  
 Gly Thr Asn Arg Ile Pro Glu Ser Gly Gly Asp Asn Ser Val Phe Asp  
 20                                      25                                      30  
 Ile Phe Glu Leu Thr Gly Ala Ala Arg Lys Gly Ser Gly Arg Arg Leu  
 35                                      40                                      45  
 Val Lys Gly Pro Asp Pro Ser Ser Pro Ala Phe Arg Ile Glu Asp Ala  
 50                                      55                                      60  
 Asn Leu Ile Pro Pro Val Pro Asp Asp Lys Phe Gln Asp Leu Val Asp



65		70		75		80
Ala Val Arg Ala Glu Lys Gly Phe Leu Leu Ala Ser Leu Arg Gln						
	85			90		95
Met Lys Lys Thr Arg Gly Thr Leu Leu Ala Leu Glu Arg Lys Asp His						
	100			105		110
Ser Gly Gln Val Phe Ser Val Val Ser Asn Gly Lys Ala Gly Thr Leu						
	115			120		125
Asp Leu Ser Leu Thr Val Gln Gly Lys Gln His Val Val Ser Val Glu						
	130			135		140
Glu Ala Leu Leu Ala Thr Gly Gln Trp Lys Ser Ile Thr Leu Phe Val						
	145			150		155
Gln Glu Asp Arg Ala Gln Leu Tyr Ile Asp Cys Glu Lys Met Glu Asn						
				165		170
Ala Glu Leu Asp Val Pro Ile Gln Ser Val Phe Thr Arg Asp Leu Ala						
				180		185
Ser Ile Ala Arg Leu Arg Ile Ala Lys Gly Gly Val Asn Asp Asn Phe						
				195		200
Gln Gly Val Leu Gln Asn Val Arg Phe Val Phe Gly Thr Thr Pro Glu						
				210		215
Asp Ile Leu Arg Asn Lys Gly Cys Ser Ser Ser Thr Ser Val Leu Leu						
				225		230
Thr Leu Asp Asn Asn Val Val Asn Gly Ser Ser Pro Ala Ile Arg Thr						
				245		250
Asn Tyr Ile Gly His Lys Thr Lys Asp Leu Gln Ala Ile Cys Gly Ile						
				260		265
Ser Cys Asp Glu Leu Ser Ser Met Val Leu Glu Leu Arg Gly Leu Arg						
				275		280
Thr Ile Val Thr Thr Leu Gln Asp Ser Ile Arg Lys Val Thr Glu Glu						
				290		295
Asn Lys Glu Leu Ala Asn Glu Leu Arg Arg Pro Pro Leu Cys Tyr His						
				305		310
Asn Gly Val Gln Tyr Arg Asn Asn Glu Glu Trp Thr Val Asp Ser Cys						
				325		330
Thr Glu Cys His Cys Gln Asn Ser Val Thr Ile Cys Lys Lys Val Ser						
				340		345
Cys Pro Ile Met Pro Cys Ser Asn Ala Thr Val Pro Asp Gly Glu Cys						
				355		360
Cys Pro Arg Cys Trp Pro Ser Asp Ser Ala Asp Asp Gly Trp Ser Pro						
				370		375
Trp Ser Glu Trp Thr Ser Cys Ser Thr Ser Cys Gly Asn Gly Ile Gln						
				385		390
						395
						400

Gln Arg Gly Arg Ser Cys Asp Ser Leu Asn Asn Arg Cys Glu Gly Ser  
 405 410 415  
 Ser Val Gln Thr Arg Thr Cys His Ile Gln Glu Cys Asp Lys Arg Phe  
 420 425 430  
 Lys Gln Asp Gly Gly Trp Ser His Trp Ser Pro Trp Ser Ser Cys Ser  
 435 440 445  
 Val Thr Cys Gly Asp Gly Val Ile Thr Arg Ile Arg Leu Cys Asn Ser  
 450 455 460  
 Pro Ser Pro Gln Met Asn Gly Lys Pro Cys Glu Gly Glu Ala Arg Glu  
 465 470 475 480  
 Thr Lys Ala Cys Lys Lys Asp Ala Cys Pro Ile Asn Gly Gly Trp Gly  
 485 490 495  
 Pro Trp Ser Pro Trp Asp Ile Cys Ser Val Thr Cys Gly Gly Gly Val  
 500 505 510  
 Gln Lys Arg Ser Arg Leu Cys Asn Asn Pro Thr Pro Gln Phe Gly Gly  
 515 520 525  
 Lys Asp Cys Val Gly Asp Val Thr Glu Asn Gln Ile Cys Asn Lys Gln  
 530 535 540  
 Asp Cys Pro Ile Gly Glu Pro Arg Ser Pro Gly  
 545 550 555

&lt;210&gt; 102

&lt;211&gt; 546

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 102

Met Gly Leu Ala Trp Gly Leu Gly Val Leu Phe Leu Met His Val Cys  
 1 5 10 15  
 Gly Thr Asn Arg Ile Pro Glu Ser Gly Gly Asp Asn Ser Val Phe Asp  
 20 25 30  
 Ile Phe Glu Leu Thr Gly Ala Ala Arg Lys Gly Ser Gly Arg Arg Leu  
 35 40 45  
 Val Lys Gly Pro Asp Pro Ser Ser Pro Ala Phe Arg Ile Glu Asp Ala  
 50 55 60  
 Asn Leu Ile Pro Pro Val Pro Asp Asp Lys Phe Gln Asp Leu Val Asp  
 65 70 75 80  
 Ala Val Arg Ala Glu Lys Gly Phe Leu Leu Leu Ala Ser Leu Arg Gln  
 85 90 95  
 Met Lys Lys Thr Arg Gly Thr Leu Leu Ala Leu Glu Arg Lys Asp His  
 100 105 110  
 Ser Gly Gln Val Phe Ser Val Val Ser Asn Gly Lys Ala Gly Thr Leu  
 115 120 125

Asp Leu Ser Leu Thr Val Gln Gly Lys Gln His Val Val Ser Val Glu  
 130 135 140  
 Glu Ala Leu Leu Ala Thr Gly Gln Trp Lys Ser Ile Thr Leu Phe Val  
 145 150 155 160  
 Gln Glu Asp Arg Ala Gln Leu Tyr Ile Asp Cys Glu Lys Met Glu Asn  
 165 170 175  
 Ala Glu Leu Asp Val Pro Ile Gln Ser Val Phe Thr Arg Asp Leu Ala  
 180 185 190  
 Ser Ile Ala Arg Leu Arg Ile Ala Lys Gly Gly Val Asn Asp Asn Phe  
 195 200 205  
 Gln Gly Val Leu Gln Asn Val Arg Phe Val Phe Gly Thr Thr Pro Glu  
 210 215 220  
 Asp Ile Leu Arg Asn Lys Gly Cys Ser Ser Ser Thr Ser Val Leu Leu  
 225 230 235 240  
 Thr Leu Asp Asn Asn Val Val Asn Gly Ser Ser Pro Ala Ile Arg Thr  
 245 250 255  
 Asn Tyr Ile Gly His Lys Thr Lys Asp Leu Gln Ala Ile Cys Gly Ile  
 260 265 270  
 Ser Cys Asp Glu Leu Ser Ser Met Val Leu Glu Leu Arg Gly Leu Arg  
 275 280 285  
 Thr Ile Val Thr Thr Leu Gln Asp Ser Ile Arg Lys Val Thr Glu Glu  
 290 295 300  
 Asn Lys Glu Leu Ala Asn Glu Leu Arg Arg Pro Pro Leu Cys Tyr His  
 305 310 315 320  
 Asn Gly Val Gln Tyr Arg Asn Asn Glu Glu Trp Thr Val Asp Ser Cys  
 325 330 335  
 Thr Glu Cys His Cys Gln Asn Ser Val Thr Ile Cys Lys Lys Val Ser  
 340 345 350  
 Cys Pro Ile Met Pro Cys Ser Asn Ala Thr Val Pro Asp Gly Glu Cys  
 355 360 365  
 Cys Pro Arg Cys Trp Pro Ser Asp Ser Ala Asp Asp Gly Trp Ser Pro  
 370 375 380  
 Trp Ser Glu Trp Thr Ser Cys Ser Thr Ser Cys Gly Asn Gly Ile Gln  
 385 390 395 400  
 Gln Arg Gly Arg Ser Cys Asp Ser Leu Asn Asn Arg Cys Glu Gly Ser  
 405 410 415  
 Ser Val Gln Thr Arg Thr Cys His Ile Gln Glu Cys Asp Lys Arg Phe  
 420 425 430  
 Lys Gln Asp Gly Gly Trp Ser His Trp Ser Pro Trp Ser Ser Cys Ser  
 435 440 445

Val Thr Cys Gly Asp Gly Val Ile Thr Arg Ile Arg Leu Cys Asn Ser  
 450 455 460

Pro Ser Pro Gln Met Asn Gly Lys Pro Cys Glu Gly Glu Ala Arg Glu  
 465 470 475 480

Thr Lys Ala Cys Lys Lys Asp Ala Cys Pro Ser Lys Cys Glu Val Arg  
 485 490 495

Cys Lys Gly Glu His Gly Gln Gln Leu Cys Pro Ala Gly Cys Leu Gly  
 500 505 510

Ile Cys Ser Leu Gln Phe Gln Trp Gly His Arg Ser Arg Lys Val Thr  
 515 520 525

Tyr Leu Gly Glu Thr Asn Arg Arg Gln Ser Pro Ala Gly Ser Ala Thr  
 530 535 540

Ser Phe  
 545

<210> 103  
 <211> 459  
 <212> PRT  
 <213> Homo sapiens

<400> 103  
 Met Gly Leu Ala Trp Gly Leu Gly Val Leu Phe Leu Met His Val Cys  
 1 5 10 15

Gly Thr Asn Arg Ile Pro Glu Ser Gly Gly Asp Asn Ser Val Phe Asp  
 20 25 30

Ile Phe Glu Leu Thr Gly Ala Ala Arg Lys Gly Ser Gly Arg Arg Leu  
 35 40 45

Val Lys Gly Pro Asp Pro Ser Ser Pro Ala Phe Arg Ile Glu Asp Ala  
 50 55 60

Asn Leu Ile Pro Pro Val Pro Asp Asp Lys Phe Gln Asp Leu Val Asp  
 65 70 75 80

Ala Val Arg Ala Glu Lys Gly Phe Leu Leu Leu Ala Ser Leu Arg Gln  
 85 90 95

Met Lys Lys Thr Arg Gly Thr Leu Leu Ala Leu Glu Arg Lys Asp His  
 100 105 110

Ser Gly Gln Val Phe Ser Val Val Ser Asn Gly Lys Ala Gly Thr Leu  
 115 120 125

Asp Leu Ser Leu Thr Val Gln Gly Lys Gln His Val Val Ser Val Glu  
 130 135 140

Glu Ala Leu Leu Ala Thr Gly Gln Trp Lys Ser Ile Thr Leu Phe Val  
 145 150 155 160

Gln Glu Asp Arg Ala Gln Leu Tyr Ile Asp Cys Glu Lys Met Glu Asn  
 165 170 175

Ala Glu Leu Asp Val Pro Ile Gln Ser Val Phe Thr Arg Asp Leu Ala  
180 185 190

Ser Ile Ala Arg Leu Arg Ile Ala Lys Gly Gly Val Asn Asp Asn Phe  
195 200 205

Gln Gly Val Leu Gln Asn Val Arg Phe Val Phe Gly Thr Thr Pro Glu  
210 215 220

Asp Ile Leu Arg Asn Lys Gly Cys Ser Ser Ser Thr Ser Val Leu Leu  
225 230 235 240

Thr Leu Asp Asn Asn Val Val Asn Gly Ser Ser Pro Ala Ile Arg Thr  
245 250 255

Asn Tyr Ile Gly His Lys Thr Lys Asp Leu Gln Ala Ile Cys Gly Ile  
260 265 270

Ser Cys Asp Glu Leu Ser Ser Met Val Leu Glu Leu Arg Gly Leu Arg  
275 280 285

Thr Ile Val Thr Thr Leu Gln Asp Ser Ile Arg Lys Val Thr Glu Glu  
290 295 300

Asn Lys Glu Leu Ala Asn Glu Leu Arg Arg Pro Pro Leu Cys Tyr His  
305 310 315 320

Asn Gly Val Gln Tyr Arg Asn Asn Glu Glu Trp Thr Val Asp Ser Cys  
325 330 335

Thr Glu Cys His Cys Gln Asn Ser Val Thr Ile Cys Lys Lys Val Ser  
340 345 350

Cys Pro Ile Met Pro Cys Ser Asn Ala Thr Val Pro Asp Gly Glu Cys  
355 360 365

Cys Pro Arg Cys Trp Pro Ser Asp Ser Ala Asp Asp Gly Trp Ser Pro  
370 375 380

Trp Ser Glu Trp Thr Ser Cys Ser Thr Ser Cys Gly Asn Gly Ile Gln  
385 390 395 400

Gln Arg Gly Arg Ser Cys Asp Ser Leu Asn Asn Arg Cys Glu Gly Ser  
405 410 415

Ser Val Gln Thr Arg Thr Cys His Ile Gln Glu Cys Asp Lys Arg Cys  
420 425 430

Lys His Leu Ser Leu Ser Gly Thr Trp Arg Thr Asp Leu Ser Leu Leu  
435 440 445

Ser Ser Pro Arg Ala Ala Pro Gln His Val Tyr  
450 455

&lt;210&gt; 104

&lt;211&gt; 363

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 104

Met Ala Ala Leu Met Thr Pro Gly Thr Gly Ala Pro Pro Ala Pro Gly  
 1 5 10 15  
 Asp Phe Ser Gly Glu Gly Ser Gln Gly Leu Pro Asp Pro Ser Pro Glu  
 20 25 30  
 Pro Lys Gln Leu Pro Glu Leu Ile Arg Met Lys Arg Asp Gly Gly Arg  
 35 40 45  
 Leu Ser Glu Ala Asp Ile Arg Gly Phe Val Ala Ala Val Val Asn Gly  
 50 55 60  
 Ser Ala Gln Gly Ala Gln Ile Gly Ala Met Leu Met Ala Ile Arg Leu  
 65 70 75 80  
 Arg Gly Met Asp Leu Glu Glu Thr Ser Val Leu Thr Gln Ala Leu Ala  
 85 90 95  
 Gln Ser Gly Gln Gln Leu Glu Trp Pro Glu Ala Trp Arg Gln Gln Leu  
 100 105 110  
 Val Asp Lys His Ser Thr Gly Gly Val Gly Asp Lys Val Ser Leu Val  
 115 120 125  
 Leu Ala Pro Ala Leu Ala Ala Cys Gly Cys Lys Val Pro Met Ile Ser  
 130 135 140  
 Gly Arg Gly Leu Gly His Thr Gly Gly Thr Leu Asp Lys Leu Glu Ser  
 145 150 155 160  
 Ile Pro Gly Phe Asn Val Ile Gln Ser Pro Glu Gln Met Gln Val Leu  
 165 170 175  
 Leu Asp Gln Ala Gly Cys Cys Ile Val Gly Gln Ser Glu Gln Leu Val  
 180 185 190  
 Pro Ala Asp Gly Ile Leu Tyr Ala Ala Arg Asp Val Thr Ala Thr Val  
 195 200 205  
 Asp Ser Leu Pro Leu Ile Thr Ala Ser Ile Leu Ser Lys Lys Leu Val  
 210 215 220  
 Glu Gly Leu Ser Ala Leu Val Val Asp Val Lys Phe Gly Gly Ala Ala  
 225 230 235 240  
 Val Phe Pro Asn Gln Glu Gln Ala Arg Glu Leu Ala Lys Thr Leu Val  
 245 250 255  
 Gly Val Gly Ala Ser Leu Gly Leu Arg Val Ala Ala Ala Leu Thr Ala  
 260 265 270  
 Met Asp Lys Pro Leu Gly Arg Cys Val Gly His Ala Leu Glu Val Glu  
 275 280 285  
 Glu Ala Leu Leu Cys Met Asp Gly Ala Gly Pro Pro Asp Leu Arg Asp  
 290 295 300  
 Leu Val Thr Thr Leu Gly Gly Ala Leu Leu Trp Leu Ser Gly His Ala  
 305 310 315 320  
 Gly Thr Gln Ala Gln Gly Ala Ala Arg Val Ala Ala Ala Arg Ala Leu

325 330 335

Gln Glu Ala Leu Val Leu Ser Asp Arg Ala Pro Phe Ala Ala Pro Ser  
340 345 350

Pro Phe Ala Glu Leu Val Leu Pro Pro Gln Gln  
355 360

<210> 105  
<211> 442  
<212> PRT  
<213> Homo sapiens

<400> 105

Met Ala Ala Leu Met Thr Pro Gly Thr Gly Ala Pro Pro Ala Pro Gly  
1 5 10 15  
Asp Phe Ser Gly Glu Gly Ser Gln Gly Leu Pro Asp Pro Ser Pro Glu  
20 25 30  
Pro Lys Gln Leu Pro Glu Leu Ile Arg Met Lys Arg Asp Gly Gly Arg  
35 40 45  
Leu Ser Glu Ala Asp Ile Arg Gly Phe Val Ala Ala Val Val Asn Gly  
50 55 60  
Ser Ala Gln Gly Ala Gln Ile Gly Ala Met Leu Met Ala Ile Arg Leu  
65 70 75 80  
Arg Gly Met Asp Leu Glu Glu Thr Ser Val Leu Thr Gln Ala Leu Ala  
85 90 95  
Gln Ser Gly Gln Gln Leu Glu Trp Pro Glu Ala Trp Arg Gln Gln Leu  
100 105 110  
Val Asp Lys His Ser Thr Gly Gly Val Gly Asp Lys Val Ser Leu Val  
115 120 125  
Leu Ala Pro Ala Leu Ala Ala Cys Gly Cys Lys Val Pro Met Ile Ser  
130 135 140  
Gly Arg Gly Leu Gly His Thr Gly Gly Thr Leu Asp Lys Leu Glu Ser  
145 150 155 160  
Ile Pro Gly Phe Asn Val Ile Gln Ser Pro Glu Gln Met Gln Val Leu  
165 170 175  
Leu Asp Gln Ala Gly Cys Cys Ile Val Gly Gln Ser Glu Gln Leu Val  
180 185 190  
Pro Ala Asp Gly Ile Leu Tyr Ala Ala Arg Asp Val Thr Ala Thr Val  
195 200 205  
Asp Ser Leu Pro Leu Ile Thr Gly Trp Arg Gly Ser Gln Pro Arg Ala  
210 215 220  
Arg Val Ala Ala Ala Leu Thr Ala Met Asp Lys Pro Leu Gly Arg Cys  
225 230 235 240  
Val Gly His Ala Leu Glu Val Glu Glu Ala Leu Leu Cys Met Asp Gly

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<210> 106
<211> 323
<212> PRT
<213> Homo sapiens
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Met Ala Ala Leu Met Thr Pro Gly Thr Gly Ala Pro Pro Ala Pro Gly  
1 5 .10 15

Asp Phe Ser Gly Glu Gly Ser Gln Gly Leu Pro Asp Pro Ser Pro Glu  
20 25 30

Pro Lys Gln Leu Pro Glu Leu Ile Arg Met Lys Arg Asp Gly Gly Arg  
35 40 45

Leu Ser Glu Ala Asp Ile Arg Gly Phe Val Ala Ala Val Val Asn Gly  
50 55 60

Ser Ala Gln Gly Ala Gln Ile Gly Ala Met Leu Met Ala Ile Arg Leu  
65 70 75 80

Arg Gly Met Asp Leu Glu Glu Thr Ser Val Leu Thr Gln Ala Leu Ala



85 90 95  
 Gln Ser Gly Gln Gln Leu Glu Trp Pro Glu Ala Trp Arg Gln Gln Leu  
 100 105 110  
 Val Asp Lys His Ser Thr Gly Gly Val Gly Asp Lys Val Ser Leu Val  
 115 120 125  
 Leu Ala Pro Ala Leu Ala Ala Cys Gly Cys Lys Val Pro Met Ile Ser  
 130 135 140  
 Gly Arg Gly Leu Gly His Thr Gly Gly Thr Leu Asp Lys Leu Glu Ser  
 145 150 155 160  
 Ile Pro Gly Phe Asn Val Ile Gln Ser Pro Glu Gln Met Gln Val Leu  
 165 170 175  
 Leu Asp Gln Ala Gly Cys Cys Ile Val Gly Gln Ser Glu Gln Leu Val  
 180 185 190  
 Pro Ala Asp Gly Ile Leu Tyr Ala Ala Arg Asp Val Thr Ala Thr Val  
 195 200 205  
 Asp Ser Leu Pro Leu Ile Thr Gly Trp Arg Gly Ser Gln Pro Arg Ala  
 210 215 220  
 Arg Val Ala Ala Ala Leu Thr Ala Met Asp Lys Pro Leu Gly Arg Cys  
 225 230 235 240  
 Val Gly His Ala Leu Glu Val Glu Glu Ala Leu Leu Cys Met Asp Gly  
 245 250 255  
 Ala Gly Pro Pro Asp Leu Arg Asp Leu Val Thr Thr Leu Gly Gly Ala  
 260 265 270  
 Leu Leu Trp Leu Ser Gly His Ala Gly Thr Gln Ala Gln Gly Ala Ala  
 275 280 285  
 Arg Val Ala Ala Ala Arg Ala Leu Gln Glu Ala Leu Val Leu Ser Asp  
 290 295 300  
 Arg Ala Pro Phe Ala Ala Pro Ser Pro Phe Ala Glu Leu Val Leu Pro  
 305 310 315 320  
 Pro Gln Gln

<210> 107  
 <211> 481  
 <212> PRT  
 <213> Homo sapiens

<400> 107  
 Met Ala Ser Arg Leu Thr Leu Leu Thr Leu Leu Leu Leu Leu Ala  
 1 5 10 15  
 Gly Asp Arg Ala Ser Ser Asn Pro Asn Ala Thr Ser Ser Val Ile Ser  
 20 25 30  
 Lys Met Leu Phe Val Glu Pro Ile Leu Glu Val Ser Ser Leu Pro Thr

35	40	45
Thr Asn Ser Thr Thr Asn Ser Ala Thr Lys Ile Thr Ala Asn Thr Thr		
50	55	60
Asp Glu Pro Thr Thr Gln Pro Thr Thr Glu Pro Thr Thr Gln Pro Thr		
65	70	75 80
Ile Gln Pro Thr Gln Pro Thr Thr Gln Leu Pro Thr Asp Ser Pro Thr		
	85	90 95
Gln Pro Thr Thr Gly Ser Phe Cys Pro Gly Pro Val Thr Leu Cys Ser		
	100	105 110
Asp Leu Glu Ser His Ser Thr Glu Ala Val Leu Gly Asp Ala Leu Val		
	115	120 125
Asp Phe Ser Leu Lys Leu Tyr His Ala Phe Ser Ala Met Lys Lys Val		
	130	135 140
Glu Thr Asn Met Ala Phe Ser Pro Phe Ser Ile Ala Ser Leu Leu Thr		
	145	150 155 160
Gln Val Leu Leu Gly Ala Gly Glu Asn Thr Lys Thr Asn Leu Glu Ser		
	165	170 175
Ile Leu Ser Tyr Pro Lys Asp Phe Thr Cys Val His Gln Ala Leu Lys		
	180	185 190
Gly Phe Thr Thr Lys Gly Val Thr Ser Val Ser Gln Ile Phe His Ser		
	195	200 205
Pro Asp Leu Ala Ile Arg Asp Thr Phe Val Asn Ala Ser Arg Thr Leu		
	210	215 220
Tyr Ser Ser Ser Pro Arg Val Leu Ser Asn Asn Ser Asp Ala Asn Leu		
	225	230 235 240
Glu Leu Ile Asn Thr Trp Val Ala Lys Asn Thr Asn Asn Lys Ile Ser		
	245	250 255
Arg Leu Leu Asp Ser Leu Pro Ser Asp Thr Arg Leu Val Leu Leu Asn		
	260	265 270
Ala Ile Tyr Leu Ser Ala Lys Trp Lys Thr Thr Phe Asp Pro Lys Lys		
	275	280 285
Thr Arg Met Glu Pro Phe His Phe Lys Asn Ser Val Ile Lys Val Pro		
	290	295 300
Met Met Asn Ser Lys Lys Tyr Pro Val Ala His Phe Ile Asp Gln Thr		
	305	310 315 320
Leu Lys Ala Lys Val Gly Gln Leu Gln Leu Ser His Asn Leu Ser Leu		
	325	330 335
Val Ile Leu Val Pro Gln Asn Leu Lys His Arg Leu Glu Asp Met Glu		
	340	345 350
Gln Ala Leu Ser Pro Ser Val Phe Lys Ala Ile Met Glu Lys Leu Glu		
	355	360 365

Met Ser Lys Phe Gln Pro Thr Leu Leu Thr Leu Pro Arg Ile Lys Val  
 370 375 380

Thr Thr Ser Gln Asp Met Leu Ser Ile Met Glu Lys Leu Glu Phe Phe  
 385 390 395 400

Asp Phe Ser Tyr Asp Leu Asn Leu Cys Gly Leu Thr Glu Asp Pro Asp  
 405 410 415

Leu Gln Val Ser Ala Met Gln His Gln Thr Val Leu Glu Leu Thr Glu  
 420 425 430

Thr Gly Val Glu Ala Ala Ala Ala Ser Ala Ile Ser Val Ala Arg Thr  
 435 440 445

Leu Leu Val Phe Glu Val Gln Gln Pro Phe Leu Phe Val Leu Trp Asp  
 450 455 460

Gln Gln His Lys Phe Pro Val Phe Met Gly Arg Val Tyr Asp Pro Arg  
 465 470 475 480

Ala

<210> 108

<211> 116

<212> PRT

<213> Homo sapiens

<400> 108

Met Met Asp Glu Glu Glu Val Glu Val Ser Leu Pro Arg Phe Lys Leu  
 1 5 10 15

Glu Glu Ser Tyr Asp Met Glu Ser Val Leu Arg Asn Leu Gly Met Thr  
 20 25 30

Asp Ala Phe Glu Leu Gly Lys Ala Asp Phe Ser Gly Met Ser Gln Thr  
 35 40 45

Asp Leu Ser Leu Ser Lys Val Val His Lys Ser Phe Val Glu Val Asn  
 50 55 60

Glu Glu Gly Thr Glu Ala Ala Ala Ala Thr Ala Ala Ile Met Met Met  
 65 70 75 80

Arg Cys Ala Arg Phe Val Pro Arg Phe Cys Ala Asp His Pro Phe Leu  
 85 90 95

Phe Phe Ile Gln His Ser Lys Thr Asn Gly Ile Leu Phe Cys Gly Arg  
 100 105 110

Phe Ser Ser Pro  
 115

<210> 109

<211> 319

<212> PRT

<213> Homo sapiens

&lt;400&gt; 109

Met Asp Val Leu Ala Glu Ala Asn Gly Thr Phe Ala Leu Asn Leu Leu  
 1 5 10 15  
 Lys Thr Leu Gly Lys Asp Asn Ser Lys Asn Val Phe Phe Ser Pro Met  
 20 25 30  
 Ser Met Ser Cys Ala Leu Ala Met Val Tyr Met Gly Ala Lys Gly Asn  
 35 40 45  
 Thr Ala Ala Gln Met Ala Gln Ile Leu Ser Phe Asn Lys Ser Gly Gly  
 50 55 60  
 Gly Gly Asp Ile His Gln Gly Phe Gln Ser Leu Leu Thr Glu Val Asn  
 65 70 75 80  
 Lys Thr Gly Thr Gln Tyr Leu Leu Arg Val Ala Asn Arg Leu Phe Gly  
 85 90 95  
 Glu Lys Ser Cys Asp Phe Leu Ser Ser Phe Arg Asp Ser Cys Gln Lys  
 100 105 110  
 Phe Tyr Gln Ala Glu Met Glu Glu Leu Asp Phe Ile Ser Ala Val Glu  
 115 120 125  
 Lys Ser Arg Lys His Ile Asn Thr Trp Val Ala Glu Lys Thr Glu Gly  
 130 135 140  
 Lys Ile Ala Glu Leu Leu Ser Pro Gly Ser Val Asp Pro Leu Thr Arg  
 145 150 155 160  
 Leu Val Leu Val Asn Ala Val Tyr Phe Arg Gly Asn Trp Asp Glu Gln  
 165 170 175  
 Phe Asp Lys Glu Asn Thr Glu Glu Arg Leu Phe Lys Val Ser Lys Asn  
 180 185 190  
 Glu Glu Lys Pro Val Gln Met Met Phe Lys Gln Ser Thr Phe Lys Lys  
 195 200 205  
 Thr Tyr Ile Gly Glu Ile Phe Thr Gln Ile Leu Val Leu Pro Tyr Val  
 210 215 220  
 Gly Lys Glu Leu Asn Met Ile Ile Met Leu Pro Asp Glu Thr Thr Asp  
 225 230 235 240  
 Leu Arg Thr Val Glu Lys Glu Leu Thr Tyr Glu Lys Phe Val Glu Trp  
 245 250 255  
 Thr Arg Leu Asp Met Met Asp Glu Glu Glu Val Glu Glu Gly Thr Glu  
 260 265 270  
 Ala Ala Ala Ala Thr Ala Ala Ile Met Met Met Arg Cys Ala Arg Phe  
 275 280 285  
 Val Pro Arg Phe Cys Ala Asp His Pro Phe Leu Phe Phe Ile Gln His  
 290 295 300  
 Ser Lys Thr Asn Gly Ile Leu Phe Cys Gly Arg Phe Ser Ser Pro  
 305 310 315

<210> 110  
 <211> 188  
 <212> PRT  
 <213> Homo sapiens

<400> 110  
 Met Asp Val Leu Ala Glu Ala Asn Gly Thr Phe Ala Leu Asn Leu Leu  
     1                    5                    10                    15  
 Lys Thr Leu Gly Lys Asp Asn Ser Lys Asn Val Phe Phe Ser Pro Met  
             20                    25                    30  
 Ser Met Ser Cys Ala Leu Ala Met Val Tyr Met Gly Ala Lys Gly Asn  
             35                    40                    45  
 Thr Ala Ala Gln Met Ala Gln Ile Leu Ser Phe Asn Lys Ser Gly Gly  
             50                    55                    60  
 Gly Gly Asp Ile His Gln Gly Phe Gln Ser Leu Leu Thr Glu Val Asn  
             65                    70                    75                    80  
 Lys Thr Gly Thr Gln Tyr Leu Leu Arg Glu Ser Tyr Asp Met Glu Ser  
                     85                    90                    95  
 Val Leu Arg Asn Leu Gly Met Thr Asp Ala Phe Glu Leu Gly Lys Ala  
                     100                    105                    110  
 Asp Phe Ser Gly Met Ser Gln Thr Asp Leu Ser Leu Ser Lys Val Val  
             115                    120                    125  
 His Lys Ser Phe Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala  
             130                    135                    140  
 Ala Thr Ala Ala Ile Met Met Met Arg Cys Ala Arg Phe Val Pro Arg  
             145                    150                    155                    160  
 Phe Cys Ala Asp His Pro Phe Leu Phe Phe Ile Gln His Ser Lys Thr  
                     165                    170                    175  
 Asn Gly Ile Leu Phe Cys Gly Arg Phe Ser Ser Pro  
             180                    185

<210> 111  
 <211> 60  
 <212> PRT  
 <213> Homo sapiens

<400> 111  
 Met Asp Val Leu Ala Glu Ala Asn Gly Thr Phe Ala Leu Asn Leu Leu  
     1                    5                    10                    15  
 Lys Thr Leu Gly Lys Asp Asn Ser Lys Asn Val Phe Phe Ser Pro Met  
             20                    25                    30  
 Ser Met Ser Cys Ala Leu Ala Met Val Tyr Met Gly Ala Lys Gly Asn  
             35                    40                    45  
 Thr Ala Ala Gln Met Ala Gln Arg Phe Gln Lys Val

50

55

60

<210> 112  
 <211> 306  
 <212> PRT  
 <213> Homo sapiens

&lt;400&gt; 112

Met His Lys Thr Ala Ser Gln Arg Leu Phe Pro Gly Pro Ser Tyr Gln  
 1 5 10 15

Asn Ile Lys Ser Ile Met Glu Asp Ser Thr Ile Leu Ser Asp Trp Thr  
 20 25 30

Asn Ser Asn Lys Gln Lys Met Lys Tyr Asp Phe Ser Cys Glu Leu Tyr  
 35 40 45

Arg Met Ser Thr Tyr Ser Thr Phe Pro Ala Gly Val Pro Val Ser Glu  
 50 55 60

Arg Ser Leu Ala Arg Ala Gly Phe Tyr Tyr Thr Gly Val Asn Asp Lys  
 65 70 75 80

Val Lys Cys Phe Cys Cys Gly Leu Met Leu Asp Asn Trp Lys Leu Gly  
 85 90 95

Asp Ser Pro Ile Gln Lys His Lys Gln Leu Tyr Pro Ser Cys Ser Phe  
 100 105 110

Ile Gln Asn Leu Val Ser Ala Ser Leu Gly Ser Thr Ser Lys Asn Thr  
 115 120 125

Ser Pro Met Arg Asn Ser Phe Ala His Ser Leu Ser Pro Thr Leu Glu  
 130 135 140

His Ser Ser Leu Phe Ser Gly Ser Tyr Ser Ser Leu Ser Pro Asn Pro  
 145 150 155 160

Leu Asn Ser Arg Ala Val Glu Asp Ile Ser Ser Ser Arg Thr Asn Pro  
 165 170 175

Tyr Ser Tyr Ala Met Ser Thr Glu Glu Ala Arg Phe Leu Thr Tyr His  
 180 185 190

Met Trp Pro Leu Thr Phe Leu Ser Pro Ser Glu Leu Ala Arg Ala Gly  
 195 200 205

Phe Tyr Tyr Ile Gly Pro Gly Asp Arg Val Ala Cys Phe Ala Cys Gly  
 210 215 220

Gly Lys Leu Ser Asn Trp Glu Pro Lys Asp Asn Ala Met Ser Glu His  
 225 230 235 240

Leu Arg His Phe Pro Asn Cys Pro Phe Leu Glu Asn Ser Leu Glu Thr  
 245 250 255

Leu Arg Phe Ser Ile Ser Asn Leu Ser Met Gln Thr His Ala Ala Arg  
 260 265 270

Met Arg Thr Phe Met Tyr Trp Pro Ser Ser Val Pro Val Gln Pro Glu

275                      280                      285  
 Gln Leu Ala Ser Ala Gly Phe Tyr Tyr Val Gly Lys Lys Leu Asn Leu  
     290                      295                      300  
  
 Leu Ile  
 305  
  
 <210> 113  
 <211> 359  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 113  
 Met His Ser Ser Met Lys Thr Ser Leu Phe Phe His Ile Val Met Gln  
     1                      5                      10                      15  
  
 Leu Gly Phe Ser Ala Leu Ser Phe Phe Tyr Pro Phe Phe Asn Ser Ser  
                     20                      25                      30  
  
 Tyr Tyr Val Gln Met Ile Ile Leu Ser Arg Phe Gly Cys Pro Asp Gln  
                     35                      40                      45  
  
 Asn Gly Asp Arg Val Glu Arg Cys Asp Ser Lys Ala Leu Asp Arg Val  
                     50                      55                      60  
  
 Ile Xaa Leu Pro Phe Ser Pro Pro Pro Arg Ser Pro Pro Asp Arg Gly  
     65                      70                      75                      80  
  
 Glu His Met Ser Ala Pro Ala Ala Lys Val Ser Lys Lys Glu Leu Asn  
                     85                      90                      95  
  
 Ser Asn His Asp Gly Ala Asp Glu Thr Ser Glu Lys Glu Gln Gln Glu  
                     100                      105                      110  
  
 Ala Ile Glu His Ile Asp Glu Val Gln Asn Glu Ile Asp Arg Leu Asn  
                     115                      120                      125  
  
 Glu Gln Ala Ser Glu Glu Ile Leu Lys Val Glu Gln Lys Tyr Asn Lys  
                     130                      135                      140  
  
 Leu Arg Gln Pro Phe Phe Gln Lys Arg Ser Glu Leu Ile Ala Lys Ile  
     145                      150                      155                      160  
  
 Pro Asn Phe Trp Val Thr Thr Phe Val Asn His Pro Gln Val Ser Ala  
                     165                      170                      175  
  
 Leu Leu Gly Glu Glu Asp Glu Glu Ala Leu His Tyr Leu Thr Arg Val  
                     180                      185                      190  
  
 Glu Val Thr Glu Phe Glu Asp Ile Lys Ser Gly Tyr Arg Ile Asp Phe  
                     195                      200                      205  
  
 Tyr Phe Asp Glu Asn Pro Tyr Phe Glu Asn Lys Val Leu Ser Lys Glu  
                     210                      215                      220  
  
 Phe His Leu Asn Glu Ser Gly Asp Pro Ser Ser Lys Ser Thr Glu Ile  
     225                      230                      235                      240  
  
 Lys Trp Lys Ser Gly Lys Asp Leu Thr Lys Arg Ser Ser Gln Thr Gln

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<210> 114
<211> 261
<212> PRT
<213> Homo sapiens
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<400> 114
Met Ser Ala Pro Ala Ala Lys Val Ser Lys Lys Glu Leu Asn Ser Asn
  1              5              10              15
His Asp Gly Ala Asp Glu Thr Ser Glu Lys Glu Gln Gln Glu Ala Ile
              20              25              30
Glu His Ile Asp Glu Val Gln Asn Glu Ile Asp Arg Leu Asn Glu Gln
              35              40              45
Ala Ser Glu Glu Ile Leu Lys Val Glu Gln Lys Tyr Asn Lys Leu Arg
              50              55              60
Gln Pro Phe Phe Gln Lys Arg Ser Glu Leu Ile Ala Lys Ile Pro Asn
              65              70              75              80
Phe Trp Val Thr Thr Phe Val Asn His Pro Gln Val Ser Ala Leu Leu
              85              90              95
Gly Glu Glu Asp Glu Glu Ala Leu His Tyr Leu Thr Arg Val Glu Val
              100              105              110
Thr Glu Phe Glu Asp Ile Lys Ser Gly Tyr Arg Ile Asp Phe Tyr Phe
              115              120              125
Asp Glu Asn Pro Tyr Phe Glu Asn Lys Val Leu Ser Lys Glu Phe His
              130              135              140
Leu Asn Glu Ser Gly Asp Pro Ser Ser Lys Ser Thr Glu Ile Lys Trp
              145              150              155              160
Lys Ser Gly Lys Asp Leu Thr Lys Arg Ser Ser Gln Thr Gln Asn Lys

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<400> 115
Met Leu Ile Ala Ala Gly Pro Ala Arg Thr Gly Val Gly Pro Ala Arg
  1                      5                      10                      15
Ile Lys Gly Ala Gln Ala Gly Trp Ala Phe His Arg Pro Ser Ala Leu
                20                      25                      30
Cys Ser Arg Gly Ala Gly Gln Ala Xaa Ala Ser Glu Leu Ala Ser Arg
          35                      40                      45
His Arg Gly Gly Ala Ala Ala Val Arg Thr Arg Gln Ala Asn Pro Thr
      50                      55                      60
Gln Lys Ser Pro Pro Pro Asp Ser Gln Val Ala Ala Ala Ser Leu Ala
  65                      70                      75                      80
His Ala Glu Ser Gly Gly Ala Gly Ser Pro Leu Arg Pro Ala Ser Ala
                85                      90                      95
Leu Ser Ser Ser Pro Phe Pro Phe Phe Ser Leu Ser Ser Pro Leu Ser
          100                      105                      110
Leu Pro Ala Phe Ala Gln Pro Arg Ala Met Ser Asp Ala Ser Leu Arg
      115                      120                      125
Ser Thr Ser Thr Met Glu Arg Leu Val Ala Arg Gly Thr Phe Pro Val
  130                      135                      140
Leu Val Arg Thr Ser Ala Cys Arg Ser Leu Phe Gly Pro Val Asp His
  145                      150                      155                      160
Glu Glu Leu Ser Arg Glu Leu Gln Ala Arg Leu Ala Glu Leu Asn Ala
                165                      170                      175
Glu Asp Gln Asn Arg Trp Asp Tyr Asp Phe Gln Gln Asp Met Pro Leu

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180 185 190  
 Arg Gly Pro Gly Arg Leu Gln Trp Thr Glu Val Asp Ser Asp Ser Val  
 195 200 205  
 Pro Ala Phe Tyr Arg Glu Thr Val Gln Ile Phe Phe Ala Lys Arg Lys  
 210 215 220  
 Arg Ser Ala Pro Glu Lys Ser Ser Gly Asp Val Pro Ala Pro Cys Pro  
 225 230 235 240  
 Ser Pro Ser Ala Ala Pro Gly Val Gly Ser Val Glu Gln Thr Pro Arg  
 245 250 255  
 Lys Arg Leu Arg  
 260

<210> 116  
 <211> 582  
 <212> PRT  
 <213> Homo sapiens

<400> 116  
 Met Met Thr Leu Arg His Leu Pro Phe Ile Leu Leu Leu Ile Leu Ser  
 1 5 10 15  
 Gly Glu Leu Tyr Ala Glu Glu Lys Gln Cys Asp Phe Pro Thr Val Glu  
 20 25 30  
 Asn Gly Arg Ile Ala Gln Tyr Tyr Tyr Thr Phe Lys Ser Phe Tyr Phe  
 35 40 45  
 Pro Met Ser Val Asp Lys Lys Leu Ser Phe Phe Cys Leu Ala Gly Tyr  
 50 55 60  
 Ala Thr Glu Ser Gly Lys Gln Glu Glu Gln Ile Arg Cys Thr Ala Glu  
 65 70 75 80  
 Gly Trp Ser Pro Asn Pro Arg Cys Tyr Lys Lys Cys Leu Lys Pro Asp  
 85 90 95  
 Leu Arg Asn Gly Tyr Val Ser Asn Asp Lys Val Leu Tyr Lys Leu Gln  
 100 105 110  
 Glu Arg Met Ser Tyr Gly Cys Ser Ser Gly Tyr Lys Thr Thr Gly Gly  
 115 120 125  
 Lys Asp Glu Glu Val Val His Cys Leu Ser Ala Gly Trp Ser Ser Gln  
 130 135 140  
 Pro Ser Cys Arg Lys Glu Gln Glu Thr Cys Leu Ala Pro Glu Leu Glu  
 145 150 155 160  
 His Gly Asn Tyr Ser Thr Thr Gln Arg Thr Phe Lys Val Lys Asp Ile  
 165 170 175  
 Val Ala Tyr Thr Cys Thr Ala Gly Tyr Tyr Thr Thr Thr Gly Lys Gln  
 180 185 190  
 Thr Gly Glu Ala Glu Cys Gln Ala Asn Gly Trp Ser Leu Thr Pro Gln

195	200	205
Cys Asn Lys Leu Met Cys Ser Ser Leu Arg Leu Ile Glu Asn Gly Tyr		
210	215	220
Phe His Pro Val Lys Gln Thr Tyr Glu Glu Gly Asp Val Val Gln Phe		
225	230	235
Phe Cys His Glu Asn Tyr Tyr Leu Ser Gly Ser Asp Leu Ile Gln Cys		
245	250	255
Tyr Asn Phe Gly Trp Tyr Pro Glu Ser Pro Ile Cys Glu Gly Arg Arg		
260	265	270
Asn Arg Cys Pro Pro Pro Pro Val Pro Leu Asn Ser Lys Ile Gln Pro		
275	280	285
His Ser Thr Thr Tyr Arg His Gly Glu Arg Val His Ile Glu Cys Glu		
290	295	300
Leu Asn Phe Val Ile Gln Gly Ser Glu Glu Leu Leu Cys Glu Asn Gly		
305	310	315
Lys Trp Thr Glu Pro Pro Lys Cys Ile Glu Glu Lys Glu Lys Val Ala		
325	330	335
Cys Glu Gln Pro Pro Ser Val Glu Asn Gly Val Ala His Pro His Ser		
340	345	350
Glu Ile Tyr Tyr Ser Gly Asp Lys Val Thr Tyr Arg Cys Gly Gly Gly		
355	360	365
Tyr Ser Leu Arg Gly Ser Ser Thr Ile Thr Cys Asn Arg Gly Arg Trp		
370	375	380
Thr Leu Pro Pro Glu Cys Val Glu Asn Ile Glu Asn Cys Lys Pro Pro		
385	390	395
Pro Asp Ile Ala Asn Gly Val Val Val Asp Gly Leu Leu Ala Ser Tyr		
405	410	415
Thr Thr Gly Ser Ser Val Glu Tyr Arg Cys Asn Glu Tyr Tyr Leu Leu		
420	425	430
Lys Gly Ser Glu Thr Ser Arg Cys Glu Gln Gly Ala Trp Ser Ser Pro		
435	440	445
Pro Val Cys Leu Glu Pro Cys Thr Ile Asp Val Asp His Met Asn Arg		
450	455	460
Asn Asn Ile Gln Leu Lys Trp Lys Tyr Glu Gly Lys Ile Leu His Gly		
465	470	475
Asp Leu Ile Asp Phe Val Cys Lys Gln Gly Tyr Asn Leu Ser Pro Ser		
485	490	495
Ile Pro Leu Ser Glu Ile Ser Ala Gln Cys Asn Arg Gly Asp Val Arg		
500	505	510
Tyr Pro Met Cys Ile Arg Lys Glu Ser Lys Gly Met Cys Ala Ser Pro		
515	520	525

Pro Val Ile Arg Asn Gly Asp Ile Val Ser Ser Ala Ala Arg Thr Tyr  
 530 535 540

Glu Asn Gly Ser Ser Val Glu Tyr Arg Cys Phe Asp Asn His Phe Leu  
 545 550 555 560

Gln Gly Ser Gln Asn Val Tyr Cys Val Asp Gly Val Trp Thr Thr Pro  
 565 570 575

Pro Ser Cys Leu Glu Pro  
 580

<210> 117

<211> 576

<212> PRT

<213> Homo sapiens

<400> 117

Met Pro Trp Gly Arg Arg Pro Thr Trp Leu Leu Leu Ala Phe Leu Leu  
 1 5 10 15

Val Phe Leu Lys Ile Ser Ile Leu Ser Val Thr Ala Trp Gln Thr Gly  
 20 25 30

Asn Cys Gln Pro Gly Pro Leu Glu Arg Ser Glu Arg Ser Gly Thr Cys  
 35 40 45

Ala Gly Pro Ala Pro Phe Leu Val Phe Ser Gln Gly Lys Ser Ile Ser  
 50 55 60

Arg Ile Trp Ala Ile Pro Ser Val Ile Arg Val Asn Lys Arg Thr Gly  
 65 70 75 80

Gln Asn Arg Val Arg Leu Gln Gly Ser Met Leu Lys Pro Ser Ser Leu  
 85 90 95

Val Val Val His Pro Leu Ala Lys Pro Gly Ala Asp Pro Cys Leu Tyr  
 100 105 110

Arg Asn Gly Gly Cys Glu His Ile Cys Gln Glu Ser Leu Gly Thr Ala  
 115 120 125

Arg Cys Leu Cys Arg Glu Gly Phe Val Lys Ala Trp Asp Gly Lys Met  
 130 135 140

Cys Leu Pro Gln Asp Tyr Pro Ile Leu Ser Gly Glu Asn Ala Asp Leu  
 145 150 155 160

Ser Lys Glu Val Thr Ser Leu Ser Asn Ser Thr Gln Ala Glu Val Pro  
 165 170 175

Asp Asp Asp Gly Thr Glu Ser Ser Thr Leu Val Ala Glu Ile Met Val  
 180 185 190

Ser Gly Met Asn Tyr Glu Asp Asp Cys Gly Pro Gly Gly Cys Gly Ser  
 195 200 205

His Ala Arg Cys Val Ser Asp Gly Glu Thr Ala Glu Cys Gln Cys Leu  
 210 215 220

Lys Gly Phe Ala Arg Asp Gly Asn Leu Cys Ser Asp Ile Asp Glu Cys  
 225 230 235 240  
 Val Leu Ala Arg Ser Asp Cys Pro Ser Thr Ser Ser Arg Cys Ile Asn  
 245 250 255  
 Thr Glu Gly Gly Tyr Val Cys Arg Cys Ser Glu Gly Tyr Glu Gly Asp  
 260 265 270  
 Gly Ile Ser Cys Phe Asp Ile Asp Glu Cys Gln Arg Gly Ala His Asn  
 275 280 285  
 Cys Ala Glu Asn Ala Ala Cys Thr Asn Thr Glu Gly Gly Tyr Asn Cys  
 290 295 300  
 Thr Cys Ala Gly Arg Pro Ser Ser Pro Gly Leu Ser Cys Pro Asp Ser  
 305 310 315 320  
 Thr Ala Pro Ser Leu Leu Gly Glu Asp Gly His His Leu Asp Arg Asn  
 325 330 335  
 Ser Tyr Pro Gly Cys Pro Ser Ser Tyr Asp Gly Tyr Cys Leu Asn Gly  
 340 345 350  
 Gly Val Cys Met His Ile Glu Ser Leu Asp Ser Tyr Thr Cys Asn Cys  
 355 360 365  
 Val Ile Gly Tyr Ser Gly Asp Arg Cys Gln Thr Arg Asp Leu Arg Trp  
 370 375 380  
 Trp Glu Leu Arg His Ala Gly Tyr Gly Gln Lys His Asp Ile Met Val  
 385 390 395 400  
 Val Ala Val Cys Met Val Ala Leu Val Leu Leu Leu Leu Gly Met  
 405 410 415  
 Trp Gly Thr Tyr Tyr Tyr Arg Thr Arg Lys Gln Leu Ser Asn Pro Pro  
 420 425 430  
 Lys Asn Pro Cys Asp Glu Pro Ser Gly Ser Val Ser Ser Ser Gly Pro  
 435 440 445  
 Asp Ser Ser Ser Gly Ala Ala Val Ala Ser Cys Pro Gln Pro Trp Phe  
 450 455 460  
 Val Val Leu Glu Lys His Gln Asp Pro Lys Asn Gly Ser Leu Pro Ala  
 465 470 475 480  
 Asp Gly Thr Asn Gly Ala Val Val Asp Ala Gly Leu Ser Pro Ser Leu  
 485 490 495  
 Gln Leu Gly Ser Val His Leu Thr Ser Trp Arg Gln Lys Pro His Ile  
 500 505 510  
 Asp Gly Met Gly Thr Gly Gln Ser Cys Trp Ile Pro Pro Ser Ser Asp  
 515 520 525  
 Arg Gly Pro Gln Glu Ile Glu Gly Asn Ser His Leu Pro Ser Tyr Arg  
 530 535 540

Pro Val Gly Pro Glu Lys Leu His Ser Leu Gln Ser Ala Asn Gly Ser  
 545 550 555 560

Cys His Glu Arg Ala Pro Asp Leu Pro Arg Gln Thr Glu Pro Val Gln  
 565 570 575

<210> 118  
 <211> 550  
 <212> PRT  
 <213> Homo sapiens

<400> 118  
 Met Pro Trp Gly Arg Arg Pro Thr Trp Leu Leu Leu Ala Phe Leu Leu  
 1 5 10 15  
 Val Phe Leu Lys Ile Ser Ile Leu Ser Val Thr Ala Trp Gln Thr Gly  
 20 25 30  
 Asn Cys Gln Pro Gly Pro Leu Glu Arg Ser Glu Arg Ser Gly Thr Cys  
 35 40 45  
 Ala Gly Pro Ala Pro Phe Leu Val Phe Ser Gln Gly Lys Ser Ile Ser  
 50 55 60  
 Arg Ile Asp Pro Asp Gly Thr Asn His Gln Gln Leu Val Val Asp Ala  
 65 70 75 80  
 Gly Ile Ser Ala Asp Met Asp Ile His Tyr Lys Lys Glu Arg Leu Tyr  
 85 90 95  
 Trp Val Asp Val Glu Arg Gln Val Leu Leu Arg Val Phe Leu Asn Gly  
 100 105 110  
 Thr Gly Leu Glu Lys Val Cys Asn Val Glu Arg Lys Val Ser Gly Leu  
 115 120 125  
 Ala Ile Asp Trp Ile Asp Asp Glu Val Leu Trp Val Asp Gln Gln Asn  
 130 135 140  
 Gly Val Ile Thr Val Thr Asp Met Thr Gly Lys Asn Ser Arg Val Leu  
 145 150 155 160  
 Leu Ser Ser Leu Lys His Pro Ser Asn Ile Ala Val Asp Pro Ile Glu  
 165 170 175  
 Arg Leu Met Phe Trp Ser Ser Glu Val Thr Gly Ser Leu His Arg Ala  
 180 185 190  
 His Leu Lys Gly Val Asp Val Lys Thr Leu Leu Glu Thr Gly Gly Ile  
 195 200 205  
 Ser Val Leu Thr Leu Asp Val Leu Asp Lys Arg Leu Phe Trp Val Gln  
 210 215 220  
 Asp Ser Gly Glu Gly Ser His Ala Tyr Ile His Ser Cys Asp Tyr Glu  
 225 230 235 240

Gly Gly Ser Val Arg Leu Ile Arg His Gln Ala Arg His Ser Leu Ser  
 245 250 255  
 Ser Met Ala Phe Phe Gly Asp Arg Ile Phe Tyr Ser Val Leu Lys Ser  
 260 265 270  
 Lys Ala Ile Trp Ile Ala Asn Lys His Thr Gly Lys Asp Thr Val Arg  
 275 280 285  
 Ile Asn Leu His Pro Ser Phe Val Thr Pro Gly Lys Leu Met Val Val  
 290 295 300  
 His Pro Arg Ala Gln Pro Arg Thr Glu Asp Ala Ala Lys Asp Pro Asp  
 305 310 315 320  
 Pro Glu Leu Leu Lys Gln Arg Gly Arg Pro Cys Arg Phe Gly Leu Cys  
 325 330 335  
 Glu Arg Asp Pro Lys Ser His Ser Ser Ala Cys Ala Glu Gly Tyr Thr  
 340 345 350  
 Leu Ser Arg Asp Arg Lys Tyr Cys Glu Asp Val Asn Glu Cys Ala Thr  
 355 360 365  
 Gln Asn His Gly Cys Thr Leu Gly Cys Glu Asn Thr Pro Gly Ser Tyr  
 370 375 380  
 His Cys Thr Cys Pro Thr Gly Phe Val Leu Leu Pro Asp Gly Lys Gln  
 385 390 395 400  
 Cys His Glu Leu Val Ser Cys Pro Gly Asn Val Ser Lys Cys Ser His  
 405 410 415  
 Gly Cys Val Leu Thr Ser Asp Gly Pro Arg Cys Ile Cys Pro Ala Gly  
 420 425 430  
 Ser Val Leu Gly Arg Asp Gly Lys Thr Cys Thr Gly Cys Ser Ser Pro  
 435 440 445  
 Asp Asn Gly Gly Cys Ser Gln Ile Cys Leu Pro Leu Arg Pro Gly Ser  
 450 455 460  
 Trp Glu Cys Asp Cys Phe Pro Gly Tyr Asp Leu Gln Ser Asp Arg Lys  
 465 470 475 480  
 Ser Cys Ala Ala Ser Gly Pro Gln Pro Leu Leu Leu Phe Ala Asn Ser  
 485 490 495  
 Gln Asp Ile Arg His Met His Phe Asp Gly Thr Asp Tyr Lys Val Leu  
 500 505 510  
 Leu Ser Arg Gln Met Gly Met Val Phe Ala Leu Asp Tyr Asp Pro Val  
 515 520 525  
 Glu Ser Lys Ile Tyr Phe Ala Gln Thr Ala Leu Lys Trp Ile Glu Arg  
 530 535 540  
 Ala Asn Met Asp Gly Ser  
 545 550

<210> 119  
 <211> 163  
 <212> PRT  
 <213> Homo sapiens

<400> 119  
 Met Pro Trp Gly Arg Arg Pro Thr Trp Leu Leu Leu Ala Phe Leu Leu  
     1                    5                    10                    15  
 Val Phe Leu Lys Ile Ser Ile Leu Ser Val Thr Ala Trp Gln Thr Gly  
                     20                    25                    30  
 Asn Cys Gln Pro Gly Pro Leu Glu Arg Ser Glu Arg Ser Gly Thr Cys  
                     35                    40                    45  
 Ala Gly Pro Ala Pro Phe Leu Val Phe Ser Gln Gly Lys Ser Ile Ser  
                     50                    55                    60  
 Arg Ile Trp Ala Ile Pro Ser Val Ile Arg Val Asn Lys Arg Thr Gly  
                     65                    70                    75                    80  
 Gln Asn Arg Val Arg Leu Gln Gly Ser Met Leu Lys Pro Ser Ser Leu  
                     85                    90                    95  
 Val Val Val His Pro Leu Ala Lys Pro Gly Ala Asp Pro Cys Leu Tyr  
                     100                    105                    110  
 Arg Asn Gly Gly Cys Glu His Ile Cys Gln Glu Ser Leu Gly Thr Ala  
                     115                    120                    125  
 Arg Cys Leu Cys Arg Glu Gly Phe Val Lys Ala Trp Asp Gly Lys Met  
                     130                    135                    140  
 Cys Leu Pro Gln Asp Tyr Pro Ile Leu Ser Gly Glu Asn Ala His Asn  
                     145                    150                    155                    160  
 Cys Ala Phe

<210> 120  
 <211> 376  
 <212> PRT  
 <213> Homo sapiens

<400> 120  
 Met Pro Trp Gly Arg Arg Pro Thr Trp Leu Leu Leu Ala Phe Leu Leu  
     1                    5                    10                    15  
 Val Ser Ala Glu Cys Gln Cys Leu Lys Gly Phe Ala Arg Asp Gly Asn  
                     20                    25                    30  
 Leu Cys Ser Asp Ile Asp Glu Cys Val Leu Ala Arg Ser Asp Cys Pro  
                     35                    40                    45  
 Ser Thr Ser Ser Arg Cys Ile Asn Thr Glu Gly Gly Tyr Val Cys Arg  
                     50                    55                    60  
 Cys Ser Glu Gly Tyr Glu Gly Asp Gly Ile Ser Cys Phe Asp Ile Asp  
                     65                    70                    75                    80



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<210> 121
<211> 444
<212> PRT
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&lt;213&gt; Homo sapiens

&lt;400&gt; 121

Met Pro Trp Gly Arg Lys Ala Trp Asp Gly Lys Met Cys Leu Pro Gln  
 1 5 10 15

Asp Tyr Pro Ile Leu Ser Gly Glu Asn Ala Asp Leu Ser Lys Glu Val  
 20 25 30

Thr Ser Leu Ser Asn Ser Thr Gln Ala Glu Val Pro Asp Asp Asp Gly  
 35 40 45

Thr Glu Ser Ser Thr Leu Val Ala Glu Ile Met Val Ser Gly Met Asn  
 50 55 60

Tyr Glu Asp Asp Cys Gly Pro Gly Gly Cys Gly Ser His Ala Arg Cys  
 65 70 75 80

Val Ser Asp Gly Glu Thr Ala Glu Cys Gln Cys Leu Lys Gly Phe Ala  
 85 90 95

Arg Asp Gly Asn Leu Cys Ser Asp Ile Asp Glu Cys Val Leu Ala Arg  
 100 105 110

Ser Asp Cys Pro Ser Thr Ser Ser Arg Cys Ile Asn Thr Glu Gly Gly  
 115 120 125

Tyr Val Cys Arg Cys Ser Glu Gly Tyr Glu Gly Asp Gly Ile Ser Cys  
 130 135 140

Phe Asp Ile Asp Glu Cys Gln Arg Gly Ala His Asn Cys Ala Glu Asn  
 145 150 155 160

Ala Ala Cys Thr Asn Thr Glu Gly Gly Tyr Asn Cys Thr Cys Ala Gly  
 165 170 175

Arg Pro Ser Ser Pro Gly Leu Ser Cys Pro Asp Ser Thr Ala Pro Ser  
 180 185 190

Leu Leu Gly Glu Asp Gly His His Leu Asp Arg Asn Ser Tyr Pro Gly  
 195 200 205

Cys Pro Ser Ser Tyr Asp Gly Tyr Cys Leu Asn Gly Gly Val Cys Met  
 210 215 220

His Ile Glu Ser Leu Asp Ser Tyr Thr Cys Asn Cys Val Ile Gly Tyr  
 225 230 235 240

Ser Gly Asp Arg Cys Gln Thr Arg Asp Leu Arg Trp Trp Glu Leu Arg  
 245 250 255

His Ala Gly Tyr Gly Gln Lys His Asp Ile Met Val Val Ala Val Cys  
 260 265 270

Met Val Ala Leu Val Leu Leu Leu Leu Gly Met Trp Gly Thr Tyr  
 275 280 285

Tyr Tyr Arg Thr Arg Lys Gln Leu Ser Asn Pro Pro Lys Asn Pro Cys  
 290 295 300

Asp Glu Pro Ser Gly Ser Val Ser Ser Ser Gly Pro Asp Ser Ser Ser

305                                      310                                      315                                      320  
 Gly Ala Ala Val Ala Ser Cys Pro Gln Pro Trp Phe Val Val Leu Glu  
    325                                      330                                      335  
 Lys His Gln Asp Pro Lys Asn Gly Ser Leu Pro Ala Asp Gly Thr Asn  
    340                                      345                                      350  
 Gly Ala Val Val Asp Ala Gly Leu Ser Pro Ser Leu Gln Leu Gly Ser  
    355                                      360                                      365  
 Val His Leu Thr Ser Trp Arg Gln Lys Pro His Ile Asp Gly Met Gly  
    370                                      375                                      380  
 Thr Gly Gln Ser Cys Trp Ile Pro Pro Ser Ser Asp Arg Gly Pro Gln  
    385                                      390                                      395                                      400  
 Glu Ile Glu Gly Asn Ser His Leu Pro Ser Tyr Arg Pro Val Gly Pro  
    405                                      410                                      415  
 Glu Lys Leu His Ser Leu Gln Ser Ala Asn Gly Ser Cys His Glu Arg  
    420                                      425                                      430  
 Ala Pro Asp Leu Pro Arg Gln Thr Glu Pro Val Gln  
    435                                      440

<210> 122  
 <211> 54  
 <212> PRT  
 <213> Homo sapiens

<400> 122  
 Met Phe Arg Glu Leu Asn Glu Ala Leu Glu Leu Lys Asp Ala His Ala  
   1   5   10   15  
 Thr Glu Glu Ser Gly Asp Ser Arg Ala His Ser Ser Tyr Leu Lys Thr  
    20   25   30  
 Lys Lys Gly Gln Ser Thr Ser Arg His Lys Lys Thr Met Val Lys Lys  
    35   40   45  
 Val Gly Pro Asp Ser Asp  
   50

<210> 123  
 <211> 855  
 <212> PRT  
 <213> Homo sapiens

<400> 123  
 Met Lys Tyr Pro Val Trp Pro Arg Tyr Ser Ala Ser Leu Gln Pro Val  
   1   5   10   15  
 Val Asp Ser Arg His Leu Thr Val Ala Thr Leu Glu Glu Arg Pro Phe  
    20   25   30  
 Val Ile Val Glu Ser Pro Asp Pro Gly Thr Gly Gly Cys Val Pro Asn  
    35   40   45

Thr Val Pro Cys Arg Arg Gln Ser Asn His Thr Phe Ser Ser Gly Asp  
 50 55 60  
 Val Ala Pro Tyr Thr Lys Leu Cys Cys Lys Gly Phe Cys Ile Asp Ile  
 65 70 75 80  
 Leu Lys Lys Leu Ala Arg Val Val Lys Phe Ser Tyr Asp Leu Tyr Leu  
 85 90 95  
 Val Thr Asn Gly Lys His Gly Lys Arg Val Arg Gly Val Trp Asn Gly  
 100 105 110  
 Met Ile Gly Glu Val Tyr Tyr Lys Arg Ala Asp Met Ala Ile Gly Ser  
 115 120 125  
 Leu Thr Ile Asn Glu Glu Arg Ser Glu Ile Val Asp Phe Ser Val Pro  
 130 135 140  
 Phe Val Glu Thr Gly Ile Ser Val Met Val Ala Arg Ser Asn Gly Thr  
 145 150 155 160  
 Val Ser Pro Ser Ala Phe Leu Glu Pro Tyr Ser Pro Ala Val Trp Val  
 165 170 175  
 Met Met Phe Val Met Cys Leu Thr Val Val Ala Ile Thr Val Phe Met  
 180 185 190  
 Phe Glu Tyr Phe Ser Pro Val Ser Tyr Asn Gln Asn Leu Thr Arg Gly  
 195 200 205  
 Lys Lys Ser Gly Gly Pro Ala Phe Thr Ile Gly Lys Ser Val Trp Leu  
 210 215 220  
 Leu Trp Ala Leu Val Phe Asn Asn Ser Val Pro Ile Glu Asn Pro Arg  
 225 230 235 240  
 Gly Thr Thr Ser Lys Ile Met Val Leu Val Trp Ala Phe Phe Ala Val  
 245 250 255  
 Ile Phe Leu Ala Ser Tyr Thr Ala Asn Leu Ala Ala Phe Met Ile Gln  
 260 265 270  
 Glu Gln Tyr Ile Asp Thr Val Ser Gly Leu Ser Asp Lys Lys Phe Gln  
 275 280 285  
 Arg Pro Gln Asp Gln Tyr Pro Pro Phe Arg Phe Gly Thr Val Pro Asn  
 290 295 300  
 Gly Ser Thr Glu Arg Asn Ile Arg Ser Asn Tyr Arg Asp Met His Thr  
 305 310 315 320  
 His Met Val Lys Phe Asn Gln Arg Ser Val Glu Asp Ala Leu Thr Ser  
 325 330 335  
 Leu Lys Met Gly Lys Leu Asp Ala Phe Ile Tyr Asp Ala Ala Val Leu  
 340 345 350  
 Asn Tyr Met Ala Gly Lys Asp Glu Gly Cys Lys Leu Val Thr Ile Gly  
 355 360 365  
 Ser Gly Lys Val Phe Ala Thr Thr Gly Tyr Gly Ile Ala Met Gln Lys

370	375	380
Asp Ser His Trp Lys Arg Ala Ile Asp Leu Ala Leu Leu Gln Phe Leu		
385	390	395 400
Gly Asp Gly Glu Thr Gln Lys Leu Glu Thr Val Trp Leu Ser Gly Ile		
	405	410 415
Cys Gln Asn Glu Lys Asn Glu Val Met Ser Ser Lys Leu Asp Ile Asp		
	420	425 430
Asn Met Ala Gly Val Phe Tyr Met Leu Leu Val Ala Met Gly Leu Ala		
	435	440 445
Leu Leu Val Phe Ala Trp Glu His Leu Val Tyr Trp Lys Leu Arg His		
	450	455 460
Ser Val Pro Asn Ser Ser Gln Leu Asp Phe Leu Leu Ala Phe Ser Arg		
	465	470 475 480
Gly Ile Tyr Ser Cys Phe Ser Gly Val Gln Ser Leu Ala Ser Pro Pro		
	485	490 495
Arg Gln Ala Ser Pro Asp Leu Thr Ala Ser Ser Ala Gln Ala Ser Val		
	500	505 510
Leu Lys Met Leu Gln Ala Ala Arg Asp Met Val Thr Thr Ala Gly Val		
	515	520 525
Ser Ser Ser Leu Asp Arg Ala Thr Arg Thr Ile Glu Asn Trp Gly Gly		
	530	535 540
Gly Arg Arg Ala Pro Pro Pro Ser Pro Cys Pro Thr Pro Arg Ser Gly		
	545	550 555 560
Pro Ser Pro Cys Leu Pro Thr Pro Asp Pro Pro Pro Glu Pro Ser Pro		
	565	570 575
Thr Gly Trp Gly Pro Pro Asp Gly Gly Arg Ala Ala Leu Val Arg Arg		
	580	585 590
Ala Pro Gln Pro Pro Gly Arg Pro Pro Thr Pro Gly Pro Pro Leu Ser		
	595	600 605
Asp Val Ser Arg Val Ser Arg Arg Pro Ala Trp Glu Ala Arg Trp Pro		
	610	615 620
Val Arg Thr Gly His Cys Gly Arg His Leu Ser Ala Ser Glu Arg Pro		
	625	630 635 640
Leu Ser Pro Ala Arg Cys His Tyr Ser Ser Phe Pro Arg Ala Asp Arg		
	645	650 655
Ser Gly Arg Pro Phe Leu Pro Leu Phe Pro Glu Pro Pro Glu Leu Glu		
	660	665 670
Asp Leu Pro Leu Leu Gly Pro Glu Gln Leu Ala Arg Arg Glu Ala Leu		
	675	680 685
Leu His Ala Ala Trp Ala Arg Gly Ser Arg Pro Arg His Ala Ser Leu		
	690	695 700

Pro Ser Ser Val Ala Glu Ala Phe Ala Arg Pro Ser Ser Leu Pro Ala  
 705 710 715 720  
 Gly Cys Thr Gly Pro Ala Cys Ala Arg Pro Asp Gly His Ser Ala Cys  
 725 730 735  
 Arg Arg Leu Ala Gln Ala Gln Ser Met Cys Leu Pro Ile Tyr Arg Glu  
 740 745 750  
 Ala Cys Gln Glu Gly Glu Gln Ala Gly Ala Pro Ala Trp Gln His Arg  
 755 760 765  
 Gln His Val Cys Leu His Ala His Ala His Leu Pro Phe Cys Trp Gly  
 770 775 780  
 Ala Val Cys Pro His Leu Pro Pro Cys Ala Ser His Gly Ser Trp Leu  
 785 790 795 800  
 Ser Gly Ala Trp Gly Pro Leu Gly His Arg Gly Arg Thr Leu Gly Leu  
 805 810 815  
 Gly Thr Gly Tyr Arg Asp Ser Gly Gly Leu Asp Glu Ile Ser Xaa Val  
 820 825 830  
 Ala Arg Gly Thr Gln Gly Phe Pro Gly Pro Cys Thr Trp Arg Arg Ile  
 835 840 845  
 Ser Ser Leu Glu Ser Glu Val  
 850 855  
  
 <210> 124  
 <211> 665  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 124  
 Met Arg Leu Ala Val Gly Ala Leu Leu Val Cys Ala Val Leu Gly Leu  
 1 5 10 15  
 Cys Leu Ala Val Pro Asp Lys Thr Val Arg Trp Cys Ala Val Ser Glu  
 20 25 30  
 His Glu Ala Thr Lys Cys Gln Ser Phe Arg Asp His Met Lys Ser Val  
 35 40 45  
 Ile Pro Ser Asp Gly Pro Ser Val Ala Cys Val Lys Lys Ala Ser Tyr  
 50 55 60  
 Leu Asp Cys Ile Arg Ala Ile Ala Ala Asn Glu Ala Asp Ala Val Thr  
 65 70 75 80  
 Leu Asp Ala Gly Leu Val Tyr Asp Ala Tyr Leu Ala Pro Asn Asn Leu  
 85 90 95  
 Lys Pro Val Val Ala Glu Phe Tyr Gly Ser Lys Glu Asp Pro Gln Thr  
 100 105 110  
 Phe Tyr Tyr Ala Val Ala Val Val Lys Lys Asp Ser Gly Phe Gln Met  
 115 120 125

Asn Gln Leu Arg Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg Ser  
 130 135 140  
 Ala Gly Trp Asn Ile Pro Ile Gly Leu Leu Tyr Cys Asp Leu Pro Glu  
 145 150 155 160  
 Pro Arg Lys Pro Leu Glu Lys Ala Val Ala Asn Phe Phe Ser Gly Ser  
 165 170 175  
 Cys Ala Pro Cys Ala Asp Gly Thr Asp Phe Pro Gln Leu Cys Gln Leu  
 180 185 190  
 Cys Pro Gly Cys Gly Cys Ser Thr Leu Asn Gln Tyr Phe Gly Tyr Ser  
 195 200 205  
 Gly Ala Phe Lys Cys Leu Lys Asp Gly Ala Gly Asp Val Ala Phe Val  
 210 215 220  
 Lys His Ser Thr Ile Phe Glu Asn Leu Ala Asn Lys Ala Asp Arg Asp  
 225 230 235 240  
 Gln Tyr Glu Leu Leu Cys Leu Asp Asn Thr Arg Lys Pro Val Asp Glu  
 245 250 255  
 Tyr Lys Asp Cys His Leu Ala Gln Val Pro Ser His Thr Val Val Ala  
 260 265 270  
 Arg Ser Met Gly Gly Lys Glu Asp Leu Ile Trp Glu Leu Leu Asn Gln  
 275 280 285  
 Ala Gln Glu His Phe Gly Lys Asp Lys Ser Lys Glu Phe Gln Leu Phe  
 290 295 300  
 Ser Ser Pro His Gly Lys Asp Leu Leu Phe Lys Asp Ser Ala His Gly  
 305 310 315 320  
 Phe Leu Lys Val Pro Pro Arg Met Asp Ala Lys Met Tyr Leu Gly Tyr  
 325 330 335  
 Glu Tyr Val Thr Ala Ile Arg Asn Leu Arg Glu Gly Thr Cys Pro Glu  
 340 345 350  
 Ala Pro Thr Asp Glu Cys Lys Pro Val Lys Trp Cys Ala Leu Ser His  
 355 360 365  
 His Glu Arg Leu Lys Cys Asp Glu Trp Ser Val Asn Ser Val Gly Lys  
 370 375 380  
 Ile Glu Cys Val Ser Ala Glu Thr Thr Glu Asp Cys Ile Ala Lys Ile  
 385 390 395 400  
 Met Asn Gly Glu Ala Asp Ala Met Ser Leu Asp Gly Gly Phe Val Tyr  
 405 410 415  
 Ile Ala Gly Lys Cys Gly Leu Val Pro Val Leu Ala Glu Asn Tyr Asn  
 420 425 430  
 Lys Ser Asp Asn Cys Glu Asp Thr Pro Glu Ala Gly Tyr Phe Ala Val  
 435 440 445

Ala Val Val Lys Lys Ser Ala Ser Asp Leu Thr Trp Asp Asn Leu Lys  
 450 455 460

Gly Lys Lys Ser Cys His Thr Ala Phe Gly Arg Thr Ala Gly Trp Asn  
 465 470 475 480

Ile Pro Met Gly Leu Leu Tyr Asn Lys Ile Asn His Cys Arg Phe Asp  
 485 490 495

Glu Phe Phe Ser Glu Gly Cys Ala Pro Gly Ser Lys Lys Asp Ser Ser  
 500 505 510

Leu Cys Lys Leu Cys Met Gly Ser Gly Leu Asn Leu Cys Glu Pro Asn  
 515 520 525

Asn Lys Glu Gly Tyr Tyr Gly Tyr Thr Gly Ala Phe Arg Cys Leu Val  
 530 535 540

Glu Lys Gly Asp Val Ala Phe Val Lys His Gln Thr Val Pro Gln Asn  
 545 550 555 560

Thr Gly Gly Lys Asn Pro Asp Pro Trp Ala Lys Asn Leu Asn Glu Lys  
 565 570 575

Asp Tyr Glu Leu Leu Cys Leu Asp Gly Thr Arg Lys Pro Val Glu Glu  
 580 585 590

Tyr Ala Asn Cys His Leu Ala Arg Ala Pro Asn His Ala Val Val Thr  
 595 600 605

Arg Lys Asp Lys Glu Ala Cys Val His Lys Ile Leu Arg Gln Gln Gln  
 610 615 620

His Leu Phe Gly Ser Asn Val Thr Asp Cys Ser Gly Asn Phe Cys Leu  
 625 630 635 640

Phe Arg Ser Glu Thr Lys Asp Leu Leu Phe Arg Asp Asp Thr His Leu  
 645 650 655

Leu Glu Ala Cys Thr Phe Arg Arg Pro :  
 660 665

&lt;210&gt; 125

&lt;211&gt; 646

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 125

Met Arg Leu Ala Val Gly Ala Leu Leu Val Cys Ala Val Leu Gly Leu  
 1 5 10 15

Cys Leu Ala Val Pro Asp Lys Thr Val Arg Trp Cys Ala Val Ser Glu  
 20 25 30

His Glu Ala Thr Lys Cys Gln Ser Phe Arg Asp His Met Lys Ser Val  
 35 40 45

Ile Pro Ser Asp Gly Pro Ser Val Ala Cys Val Lys Lys Ala Ser Tyr  
 50 55 60



Leu Asp Cys Ile Arg Ala Ile Ala Ala Asn Glu Ala Asp Ala Val Thr  
 65 70 75 80  
 Leu Asp Ala Gly Leu Val Tyr Asp Ala Tyr Leu Ala Pro Asn Asn Leu  
 85 90 95  
 Lys Pro Val Val Ala Glu Phe Tyr Gly Ser Lys Glu Asp Pro Gln Thr  
 100 105 110  
 Phe Tyr Tyr Ala Val Ala Val Val Lys Lys Asp Ser Gly Phe Gln Met  
 115 120 125  
 Asn Gln Leu Arg Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg Ser  
 130 135 140  
 Ala Gly Trp Asn Ile Pro Ile Gly Leu Leu Tyr Cys Asp Leu Pro Glu  
 145 150 155 160  
 Pro Arg Lys Pro Leu Glu Lys Ala Val Ala Asn Phe Phe Ser Gly Ser  
 165 170 175  
 Cys Ala Pro Cys Ala Asp Gly Thr Asp Phe Pro Gln Leu Cys Gln Leu  
 180 185 190  
 Cys Pro Gly Cys Gly Cys Ser Thr Leu Asn Gln Tyr Phe Gly Tyr Ser  
 195 200 205  
 Gly Ala Phe Lys Cys Leu Lys Asp Gly Ala Gly Asp Val Ala Phe Val  
 210 215 220  
 Lys His Ser Thr Ile Phe Glu Asn Leu Ala Asn Lys Ala Asp Arg Asp  
 225 230 235 240  
 Gln Tyr Glu Leu Leu Cys Leu Asp Asn Thr Arg Lys Pro Val Asp Glu  
 245 250 255  
 Tyr Lys Asp Cys His Leu Ala Gln Val Pro Ser His Thr Val Val Ala  
 260 265 270  
 Arg Ser Met Gly Gly Lys Glu Asp Leu Ile Trp Glu Leu Leu Asn Gln  
 275 280 285  
 Ala Gln Glu His Phe Gly Lys Asp Lys Ser Lys Glu Phe Gln Leu Phe  
 290 295 300  
 Ser Ser Pro His Gly Lys Asp Leu Leu Phe Lys Asp Ser Ala His Gly  
 305 310 315 320  
 Phe Leu Lys Val Pro Pro Arg Met Asp Ala Lys Met Tyr Leu Gly Tyr  
 325 330 335  
 Glu Tyr Val Thr Ala Ile Arg Asn Leu Arg Glu Gly Thr Cys Pro Glu  
 340 345 350  
 Ala Pro Thr Asp Glu Cys Lys Pro Val Lys Trp Cys Ala Leu Ser His  
 355 360 365  
 His Glu Arg Leu Lys Cys Asp Glu Trp Ser Val Asn Ser Val Gly Lys  
 370 375 380  
 Ile Glu Cys Val Ser Ala Glu Thr Thr Glu Asp Cys Ile Ala Lys Ile

385		390		395		400
Met Asn Gly Glu Ala Asp Ala Met Ser Leu Asp Gly Gly Phe Val Tyr						
	405			410		415
Ile Ala Gly Lys Cys Gly Leu Val Pro Val Leu Ala Glu Asn Tyr Asn						
	420		425			430
Lys Ser Asp Asn Cys Glu Asp Thr Pro Glu Ala Gly Tyr Phe Ala Glu						
	435		440			445
Glu Gly Cys Ala Pro Gly Ser Lys Lys Asp Ser Ser Leu Cys Lys Leu						
	450		455			460
Cys Met Gly Ser Gly Leu Asn Leu Cys Glu Pro Asn Asn Lys Glu Gly						
465		470		475		480
Tyr Tyr Gly Tyr Thr Gly Ala Phe Arg Cys Leu Val Glu Lys Gly Asp						
	485		490			495
Val Ala Phe Val Lys His Gln Thr Val Pro Gln Asn Thr Gly Gly Lys						
	500		505			510
Asn Pro Asp Pro Trp Ala Lys Asn Leu Asn Glu Lys Asp Tyr Glu Leu						
	515		520			525
Leu Cys Leu Asp Gly Thr Arg Lys Pro Val Glu Glu Tyr Ala Asn Cys						
	530		535			540
His Leu Ala Arg Ala Pro Asn His Ala Val Val Thr Arg Lys Asp Lys						
545		550		555		560
Glu Ala Cys Val His Lys Ile Leu Arg Gln Gln Gln His Leu Phe Gly						
	565		570			575
Ser Asn Val Thr Asp Cys Ser Gly Asn Phe Cys Leu Phe Arg Ser Glu						
	580		585			590
Thr Lys Asp Leu Leu Phe Arg Asp Asp Thr Val Cys Leu Ala Lys Leu						
	595		600			605
His Asp Arg Asn Thr Tyr Glu Lys Tyr Leu Gly Glu Glu Tyr Val Lys						
	610		615			620
Ala Val Gly Asn Leu Arg Lys Cys Ser Thr Ser Ser Leu Leu Glu Ala						
625		630		635		640
Cys Thr Phe Arg Arg Pro						
	645					

&lt;210&gt; 126

&lt;211&gt; 4787

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 126

Met	Ala	Glu	Gly	Gly	Glu	Gly	Gly	Glu	Asp	Glu	Ile	Gln	Phe	Leu	Arg
1				5				10						15	

Thr Glu Asp Glu Val Val Leu Gln Cys Ile Ala Thr Ile His Lys Glu

20	25	30
Gln Arg Lys Phe Cys Leu Ala Ala Glu Gly Leu Gly Asn Arg Leu Cys		
35	40	45
Phe Leu Glu Pro Thr Ser Glu Ala Lys Tyr Ile Pro Pro Asp Leu Cys		
50	55	60
Val Cys Asn Phe Val Leu Glu Gln Ser Leu Ser Val Arg Ala Leu Gln		
65	70	75
Glu Met Leu Ala Asn Thr Gly Glu Asn Gly Gly Glu Gly Ala Ala Gln		
85	90	95
Gly Gly Gly His Arg Thr Leu Leu Tyr Gly His Ala Val Leu Leu Arg		
100	105	110
His Ser Phe Ser Gly Met Tyr Leu Thr Cys Leu Thr Thr Ser Arg Ser		
115	120	125
Gln Thr Asp Lys Leu Ala Phe Asp Val Gly Leu Arg Glu His Ala Thr		
130	135	140
Gly Glu Ala Cys Trp Trp Thr Ile His Pro Ala Ser Lys Gln Arg Ser		
145	150	155
Glu Gly Glu Lys Val Arg Ile Gly Asp Asp Leu Ile Leu Val Ser Val		
165	170	175
Ser Ser Glu Arg Tyr Leu His Leu Ser Val Ser Asn Gly Asn Ile Gln		
180	185	190
Val Asp Ala Ser Phe Met Gln Thr Leu Trp Asn Val His Pro Thr Cys		
195	200	205
Ser Gly Ser Ser Ile Glu Glu Gly Tyr Leu Leu Gly Gly His Val Val		
210	215	220
Arg Leu Phe His Gly His Asp Glu Cys Leu Thr Ile Pro Ser Thr Asp		
225	230	235
Gln Asn Asp Ser Gln His Arg Arg Ile Phe Tyr Glu Ala Gly Gly Ala		
245	250	255
Gly Thr Arg Ala Xaa Ser Leu Trp Arg Val Glu Pro Leu Arg Ile Ser		
260	265	270
Trp Ser Gly Ser Asn Ile Arg Trp Gly Gln Ala Phe Arg Leu Arg His		
275	280	285
Leu Thr Thr Gly His Tyr Leu Ala Leu Thr Glu Asp Gln Gly Leu Ile		
290	295	300
Leu Gln Asp Arg Ala Lys Ser Asp Thr Lys Ser Thr Ala Phe Ser Phe		
305	310	315
Arg Ala Ser Lys Glu Leu Lys Glu Lys Leu Asp Ser Ser His Lys Arg		
325	330	335
Asp Ile Glu Gly Met Gly Val Pro Glu Ile Lys Tyr Gly Asp Ser Val		
340	345	350

Cys Phe Val Gln His Ile Ala Ser Gly Leu Trp Val Thr Tyr Lys Ala  
 355 360 365  
 Gln Asp Ala Lys Thr Ser Arg Leu Gly Pro Leu Lys Arg Lys Val Ile  
 370 375 380  
 Leu His Gln Glu Gly His Met Asp Asp Gly Leu Thr Leu Gln Arg Cys  
 385 390 395 400  
 Gln Arg Glu Glu Ser Gln Ala Ala Arg Ile Ile Arg Asn Thr Thr Ala  
 405 410 415  
 Leu Phe Ser Gln Phe Val Ser Gly Asn Asn Arg Thr Ala Ala Pro Ile  
 420 425 430  
 Thr Leu Pro Ile Glu Glu Val Leu Gln Thr Leu Gln Asp Leu Ile Ala  
 435 440 445  
 Tyr Phe Gln Pro Pro Glu Glu Glu Met Arg His Glu Asp Lys Gln Asn  
 450 455 460  
 Lys Leu Arg Ser Leu Lys Asn Arg Gln Asn Leu Phe Lys Glu Glu Gly  
 465 470 475 480  
 Met Leu Ala Leu Val Leu Asn Cys Ile Asp Arg Leu Asn Xaa Tyr Asn  
 485 490 495  
 Ser Val Ala His Phe Ala Gly Ile Ala Arg Glu Glu Ser Gly Met Ala  
 500 505 510  
 Trp Lys Glu Ile Leu Asn Leu Leu Tyr Lys Leu Leu Ala Ala Leu Ile  
 515 520 525  
 Arg Gly Asn Arg Asn Asn Cys Ala Gln Phe Ser Asn Asn Leu Asp Trp  
 530 535 540  
 Leu Ile Ser Lys Leu Asp Arg Leu Glu Ser Ser Ser Gly Ile Leu Glu  
 545 550 555 560  
 Val Leu His Cys Ile Leu Thr Glu Ser Pro Glu Ala Leu Asn Leu Ile  
 565 570 575  
 Ala Glu Gly His Ile Lys Ser Ile Ile Ser Leu Leu Asp Lys His Gly  
 580 585 590  
 Arg Asn His Lys Val Leu Asp Ile Leu Cys Ser Leu Cys Leu Cys Asn  
 595 600 605  
 Gly Val Ala Val Arg Ala Asn Gln Asn Leu Ile Cys Asp Asn Leu Leu  
 610 615 620  
 Pro Arg Arg Asn Leu Leu Leu Gln Thr Arg Leu Ile Asn Asp Val Thr  
 625 630 635 640  
 Ser Ile Arg Pro Asn Ile Phe Leu Gly Val Ala Glu Gly Ser Ala Gln  
 645 650 655  
 Tyr Lys Lys Trp Tyr Phe Glu Leu Ile Ile Asp Gln Val Asp Pro Phe  
 660 665 670

Leu Thr Ala Glu Pro Thr His Leu Arg Val Gly Trp Ala Ser Ser Ser  
 675 680 685  
 Gly Tyr Ala Pro Xaa Pro Gly Gly Gly Glu Gly Trp Gly Gly Asn Gly  
 690 695 700  
 Val Gly Asp Asp Leu Tyr Ser Tyr Gly Phe Asp Gly Leu His Leu Trp  
 705 710 715 720  
 Ser Gly Arg Ile Pro Arg Ala Val Ala Ser Xaa Asn Gln His Leu Leu  
 725 730 735  
 Arg Ser Asp Asp Val Val Ser Cys Cys Leu Asp Leu Gly Cys Pro Ala  
 740 745 750  
 Ser His Ser Ala Ser Met Gly Ser Pro Cys Arg Gly Cys Leu Arg Asn  
 755 760 765  
 Phe Asn Thr Asp Gly Leu Phe Phe Pro Val Met Ser Phe Ser Ala Gly  
 770 775 780  
 Val Lys Val Arg Phe Leu Met Gly Gly Arg His Gly Glu Phe Lys Phe  
 785 790 795 800  
 Leu Pro Pro Ser Gly Tyr Ala Pro Cys Tyr Glu Ala Leu Leu Pro Lys  
 805 810 815  
 Glu Lys Met Arg Leu Glu Pro Val Lys Glu Tyr Lys Arg Asp Ala Asp  
 820 825 830  
 Gly Ile Arg Asp Leu Leu Gly Thr Thr Gln Phe Leu Ser Gln Ala Ser  
 835 840 845  
 Phe Ile Pro Cys Pro Val Asp Thr Ser Gln Val Ile Leu Pro Pro His  
 850 855 860  
 Leu Glu Lys Ile Arg Asp Arg Leu Ala Glu Asn Ile His Glu Leu Trp  
 865 870 875 880  
 Gly Met Asn Lys Ile Glu Leu Gly Trp Thr Phe Gly Lys Ile Arg Asp  
 885 890 895  
 Asp Asn Lys Arg Gln His Pro Cys Leu Val Glu Phe Ser Lys Leu Pro  
 900 905 910  
 Glu Thr Glu Lys Asn Tyr Asn Leu Gln Met Ser Thr Glu Thr Leu Lys  
 915 920 925  
 Thr Leu Leu Xaa Leu Gly Cys His Ile Ala His Val Asn Pro Ala Ala  
 930 935 940  
 Glu Glu Asp Leu Lys Lys Val Lys Leu Pro Lys Asn Tyr Met Met Ser  
 945 950 955 960  
 Asn Gly Tyr Lys Pro Ala Pro Leu Asp Leu Ser Asp Val Lys Leu Leu  
 965 970 975  
 Pro Pro Gln Glu Ile Leu Val Asp Lys Leu Ala Glu Asn Ala His Asn  
 980 985 990  
 Val Trp Ala Lys Asp Arg Ile Lys Gln Gly Trp Thr Tyr Gly Ile Gln

995	1000	1005
Gln Asp Leu Lys Asn Lys Arg Asn Pro Arg Leu Val Pro Tyr Ala Leu		
1010	1015	1020
Leu Asp Glu Arg Thr Lys Lys Ser Asn Arg Asp Ser Leu Arg Glu Ala		
1025	1030	1035 1040
Val Arg Thr Phe Val Gly Tyr Gly Tyr Asn Ile Glu Pro Ser Asp Gln		
	1045	1050 1055
Glu Leu Ala Asp Ser Ala Val Glu Lys Val Ser Ile Asp Lys Ile Arg		
	1060	1065 1070
Phe Phe Arg Val Glu Arg Ser Tyr Xaa Val Arg Ser Gly Lys Trp Tyr		
	1075	1080 1085
Phe Glu Phe Glu Val Val Thr Gly Gly Asp Met Arg Val Gly Trp Ala		
	1090	1095 1100
Arg Pro Gly Cys Arg Pro Asp Val Glu Leu Gly Ala Asp Asp Gln Ala		
	1105	1110 1115 1120
Phe Val Phe Glu Gly Asn Arg Gly Gln Arg Trp His Gln Gly Ser Gly		
	1125	1130 1135
Tyr Phe Gly Arg Thr Trp Gln Pro Gly Asp Val Val Gly Cys Met Ile		
	1140	1145 1150
Asn Leu Asp Asp Ala Ser Met Ile Phe Thr Leu Asn Gly Glu Leu Leu		
	1155	1160 1165
Ile Thr Asn Lys Gly Ser Glu Leu Ala Phe Ala Asp Tyr Glu Ile Glu		
	1170	1175 1180
Asn Gly Phe Val Pro Ile Cys Cys Leu Gly Leu Ser Gln Ile Gly Arg		
	1185	1190 1195 1200
Met Asn Leu Gly Thr Asp Ala Ser Thr Phe Lys Phe Tyr Thr Met Cys		
	1205	1210 1215
Gly Leu Gln Glu Gly Phe Glu Pro Phe Ala Val Asn Met Asn Arg Asp		
	1220	1225 1230
Val Ala Met Trp Phe Ser Lys Arg Leu Pro Thr Phe Val Asn Val Pro		
	1235	1240 1245
Lys Asp His Pro His Ile Glu Val Met Arg Ile Asp Gly Thr Met Asp		
	1250	1255 1260
Ser Pro Pro Cys Leu Lys Val Thr His Lys Thr Phe Gly Thr Gln Asn		
	1265	1270 1275 1280
Ser Asn Ala Asp Met Ile Tyr Cys Arg Leu Ser Met Pro Val Glu Cys		
	1285	1290 1295
His Ser Ser Phe Ser His Ser Pro Cys Leu Asp Ser Glu Ala Phe Gln		
	1300	1305 1310
Lys Arg Lys Gln Met Gln Glu Ile Leu Ser His Thr Thr Thr Gln Cys		
	1315	1320 1325

Tyr Tyr Ala Ile Arg Ile Phe Xaa Gly Gln Asp Pro Ser Cys Val Trp  
 1330 1335 1340  
 Val Gly Trp Val Thr Pro Asp Tyr His Leu Tyr Ser Glu Lys Phe Asp  
 1345 1350 1355 1360  
 Leu Asn Lys Asn Cys Thr Val Thr Val Thr Leu Gly Asp Glu Arg Gly  
 1365 1370 1375  
 Arg Val His Glu Ser Val Lys Arg Ser Asn Cys Tyr Met Val Trp Gly  
 1380 1385 1390  
 Gly Asp Ile Val Ala Ser Ser Gln Arg Ser Asn Arg Ser Asn Val Asp  
 1395 1400 1405  
 Leu Glu Ile Gly Cys Leu Val Asp Leu Ala Met Gly Met Leu Ser Phe  
 1410 1415 1420  
 Ser Ala Asn Gly Lys Glu Leu Gly Thr Cys Tyr Gln Val Glu Pro Asn  
 1425 1430 1435 1440  
 Thr Lys Val Phe Pro Ala Val Phe Leu Gln Pro Thr Ser Thr Ser Leu  
 1445 1450 1455  
 Phe Gln Phe Glu Leu Gly Lys Leu Lys Asn Ala Met Pro Leu Ser Ala  
 1460 1465 1470  
 Ala Ile Phe Arg Ser Glu Glu Xaa Asn Pro Val Pro Gln Cys Pro Pro  
 1475 1480 1485  
 Arg Leu Asp Val Gln Thr Ile Gln Pro Val Leu Trp Ser Arg Met Pro  
 1490 1495 1500  
 Asn Ser Phe Leu Lys Val Glu Thr Glu Arg Val Ser Glu Arg His Gly  
 1505 1510 1515 1520  
 Trp Val Val Gln Cys Leu Glu Pro Leu Gln Met Met Ala Leu His Ile  
 1525 1530 1535  
 Pro Glu Glu Asn Arg Cys Val Asp Ile Leu Glu Leu Cys Glu Gln Glu  
 1540 1545 1550  
 Asp Leu Met Arg Phe His Tyr His Thr Leu Arg Leu Tyr Ser Ala Val  
 1555 1560 1565  
 Cys Ala Leu Gly Asn Ser Arg Val Ala Tyr Ala Leu Cys Ser His Val  
 1570 1575 1580  
 Asp Leu Ser Gln Leu Phe Tyr Ala Ile Asp Asn Lys Tyr Leu Pro Gly  
 1585 1590 1595 1600  
 Leu Leu Arg Ser Gly Phe Tyr Asp Leu Leu Ile Ser Ile His Leu Ala  
 1605 1610 1615  
 Ser Ala Lys Glu Arg Lys Leu Met Met Lys Asn Glu Tyr Ile Ile Pro  
 1620 1625 1630  
 Ile Thr Ser Thr Thr Arg Asn Ile Cys Leu Phe Pro Asp Glu Ser Lys  
 1635 1640 1645

Arg His Gly Leu Pro Gly Val Gly Leu Arg Thr Cys Leu Lys Pro Gly  
 1650 1655 1660  
 Phe Arg Phe Ser Thr Pro Cys Phe Val Val Thr Gly Glu Asp His Gln  
 1665 1670 1675 1680  
 Lys Gln Ser Pro Glu Ile Pro Leu Glu Ser Leu Arg Thr Lys Ala Leu  
 1685 1690 1695  
 Ser Met Leu Thr Glu Ala Val Gln Cys Ser Gly Ala His Ile Arg Asp  
 1700 1705 1710  
 Pro Val Gly Gly Ser Val Glu Phe Gln Phe Val Pro Val Leu Lys Leu  
 1715 1720 1725  
 Ile Gly Thr Leu Leu Val Met Gly Val Phe Asp Asp Asp Asp Val Arg  
 1730 1735 1740  
 Gln Ile Leu Leu Leu Ile Asp Pro Ser Val Phe Gly Glu His Ser Ala  
 1745 1750 1755 1760  
 Gly Thr Glu Glu Gly Ala Glu Lys Glu Glu Val Thr Gln Val Glu Glu  
 1765 1770 1775  
 Lys Ala Val Glu Ala Gly Glu Lys Ala Gly Lys Glu Ala Pro Val Lys  
 1780 1785 1790  
 Gly Leu Leu Gln Thr Arg Leu Pro Glu Ser Val Lys Leu Gln Met Cys  
 1795 1800 1805  
 Glu Leu Leu Ser Tyr Leu Cys Asp Cys Glu Leu Gln His Arg Val Glu  
 1810 1815 1820  
 Ala Ile Val Ala Phe Gly Asp Ile Tyr Val Ser Lys Leu Gln Ala Asn  
 1825 1830 1835 1840  
 Gln Lys Phe Arg Tyr Asn Glu Leu Met Gln Ala Leu Asn Met Ser Ala  
 1845 1850 1855  
 Ala Leu Thr Ala Arg Lys Thr Lys Glu Phe Arg Ser Pro Pro Gln Glu  
 1860 1865 1870  
 Gln Ile Asn Met Leu Leu Asn Phe Gln Leu Gly Glu Asn Cys Pro Cys  
 1875 1880 1885  
 Pro Glu Glu Ile Arg Glu Glu Leu Tyr Asp Phe His Glu Asp Leu Leu  
 1890 1895 1900  
 Leu His Cys Gly Val Pro Leu Glu Glu Glu Glu Glu Glu Glu Asp  
 1905 1910 1915 1920  
 Thr Ser Trp Thr Gly Lys Leu Cys Ala Leu Val Tyr Lys Ile Lys Gly  
 1925 1930 1935  
 Pro Pro Lys Pro Glu Lys Glu Gln Pro Thr Glu Glu Glu Glu Arg Cys  
 1940 1945 1950  
 Pro Thr Thr Leu Lys Glu Leu Ile Ser Gln Thr Met Ile Cys Trp Ala  
 1955 1960 1965  
 Gln Glu Asp Gln Ile Gln Asp Ser Glu Leu Val Arg Met Met Phe Asn



1970	1975	1980
Leu Leu Arg Arg Gln Tyr Asp Ser Ile Gly Glu Leu Leu Gln Ala Leu 1985	1990	1995 2000
Arg Lys Thr Tyr Thr Ile Ser His Thr Ser Val Ser Asp Thr Ile Asn 2005	2010	2015
Leu Leu Ala Ala Leu Gly Gln Ile Arg Ser Leu Leu Ser Val Arg Met 2020	2025	2030
Gly Lys Glu Glu Glu Leu Leu Met Ile Asn Gly Leu Gly Asp Ile Met 2035	2040	2045
Asn Asn Lys Val Phe Tyr Gln His Pro Asn Leu Met Arg Val Leu Gly 2050	2055	2060
Met His Glu Thr Val Met Glu Val Met Val Asn Val Leu Gly Thr Glu 2065	2070	2075 2080
Lys Ser Gln Ile Ala Phe Pro Lys Met Val Ala Ser Cys Cys Arg Phe 2085	2090	2095
Leu Cys Tyr Phe Cys Arg Ile Ser Arg Gln Asn Gln Lys Ala Met Phe 2100	2105	2110
Glu His Leu Ser Tyr Leu Leu Glu Asn Ser Ser Val Gly Leu Ala Ser 2115	2120	2125
Pro Ser Met Arg Gly Ser Thr Pro Leu Asp Val Ala Ala Ser Ser Val 2130	2135	2140
Met Asp Asn Asn Glu Leu Ala Leu Ser Leu Glu Glu Pro Asp Leu Glu 2145	2150	2155 2160
Lys Val Val Thr Tyr Leu Ala Gly Cys Gly Leu Gln Ser Cys Pro Met 2165	2170	2175
Leu Leu Ala Lys Gly Tyr Pro Asp Val Gly Trp Asn Pro Ile Glu Gly 2180	2185	2190
Glu Arg Tyr Leu Ser Phe Leu Arg Phe Ala Val Phe Val Asn Ser Glu 2195	2200	2205
Ser Val Glu Glu Asn Ala Ser Val Val Val Lys Leu Leu Ile Arg Arg 2210	2215	2220
Pro Glu Cys Phe Gly Pro Ala Leu Arg Gly Glu Gly Gly Asn Gly Leu 2225	2230	2235 2240
Leu Ala Ala Met Gln Gly Ala Ile Lys Ile Ser Glu Asn Pro Ala Leu 2245	2250	2255
Asp Leu Pro Ser Gln Gly Tyr Lys Arg Glu Val Ser Thr Glu Asp Asp 2260	2265	2270
Glu Glu Glu Glu Glu Ile Val His Met Gly Asn Ala Ile Met Ser Phe 2275	2280	2285
Tyr Ser Ala Leu Ile Asp Leu Leu Gly Arg Cys Ala Pro Glu Met His 2290	2295	2300

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Ser His Asp Lys Trp Ala Cys Asp Lys Ser Gln Ser Gly Trp Lys Tyr  
 2625 2630 2635 2640  
 Gly Ile Ser Leu Asp Glu Asn Val Lys Thr His Pro Leu Ile Arg Pro  
 2645 2650 2655  
 Phe Lys Thr Leu Thr Glu Lys Glu Lys Glu Ile Tyr Arg Trp Pro Ala  
 2660 2665 2670  
 Arg Glu Ser Leu Lys Thr Met Leu Ala Val Gly Trp Thr Val Glu Arg  
 2675 2680 2685  
 Thr Lys Glu Gly Glu Ala Leu Val Gln Gln Arg Glu Asn Glu Lys Leu  
 2690 2695 2700  
 Arg Ser Val Ser Gln Ala Asn Gln Gly Asn Ser Tyr Ser Pro Ala Pro  
 2705 2710 2715 2720  
 Leu Asp Leu Ser Asn Val Val Leu Ser Arg Glu Leu Gln Gly Met Val  
 2725 2730 2735  
 Glu Val Val Ala Glu Asn Tyr His Asn Ile Trp Ala Lys Lys Lys Lys  
 2740 2745 2750  
 Leu Glu Leu Glu Ser Lys Gly Gly Gly Ser His Pro Leu Leu Val Pro  
 2755 2760 2765  
 Tyr Asp Thr Leu Thr Ala Lys Glu Lys Phe Lys Asp Arg Glu Lys Ala  
 2770 2775 2780  
 Gln Asp Leu Phe Lys Phe Leu Gln Val Asn Gly Ile Ile Val Ser Arg  
 2785 2790 2795 2800  
 Gly Met Lys Asp Met Glu Leu Asp Ala Ser Ser Met Glu Lys Arg Phe  
 2805 2810 2815  
 Xaa Tyr Lys Phe Leu Lys Lys Ile Leu Lys Tyr Val Asp Ser Ala Gln  
 2820 2825 2830  
 Glu Phe Ile Ala His Leu Glu Ala Ile Val Ser Ser Gly Lys Thr Glu  
 2835 2840 2845  
 Lys Ser Pro Arg Asp Gln Glu Ile Lys Phe Phe Ala Lys Val Leu Leu  
 2850 2855 2860  
 Pro Leu Val Asp Gln Tyr Phe Thr Ser His Cys Leu Tyr Phe Leu Ser  
 2865 2870 2875 2880  
 Ser Pro Leu Lys Pro Leu Ser Ser Ser Gly Tyr Ala Ser His Lys Glu  
 2885 2890 2895  
 Lys Glu Met Val Ala Gly Leu Phe Cys Lys Leu Ala Ala Leu Val Arg  
 2900 2905 2910  
 His Arg Ile Ser Leu Phe Gly Ser Asp Ser Thr Thr Met Val Ser Cys  
 2915 2920 2925  
 Leu His Ile Leu Ala Gln Thr Leu Asp Thr Arg Thr Val Met Lys Ser  
 2930 2935 2940  
 Gly Ser Glu Leu Val Lys Ala Gly Leu Arg Ala Phe Phe Glu Asn Ala

2945                      2950                      2955                      2960  
 Ala Glu Asp Leu Glu Lys Thr Ser Glu Asn Leu Lys Leu Gly Lys Phe  
                                  2965                      2970                      2975  
 Thr His Ser Arg Thr Gln Ile Lys Gly Val Ser Gln Asn Ile Asn Tyr  
                                  2980                      2985                      2990  
 Thr Thr Val Ala Leu Leu Pro Ile Leu Thr Ser Ile Phe Glu His Val  
                                  2995                      3000                      3005  
 Thr Gln His Gln Phe Gly Met Asp Leu Leu Leu Gly Asp Val Gln Ile  
                                  3010                      3015                      3020  
 Ser Cys Tyr His Ile Leu Cys Ser Leu Tyr Ser Leu Gly Thr Gly Lys  
                                  3025                      3030                      3035                      3040  
 Asn Ile Tyr Val Glu Arg Gln Arg Pro Ala Leu Gly Glu Cys Leu Ala  
                                  3045                      3050                      3055  
 Ser Leu Ala Ala Ala Ile Pro Val Ala Phe Leu Glu Pro Thr Leu Asn  
                                  3060                      3065                      3070  
 Arg Tyr Asn Pro Leu Ser Val Phe Asn Thr Lys Thr Pro Arg Glu Arg  
                                  3075                      3080                      3085  
 Ser Ile Leu Gly Met Pro Asp Thr Val Glu Asp Met Cys Pro Asp Ile  
                                  3090                      3095                      3100  
 Pro Gln Leu Glu Gly Leu Met Lys Glu Ile Asn Asp Leu Ala Glu Ser  
                                  3105                      3110                      3115                      3120  
 Gly Ala Arg Tyr Thr Glu Met Pro His Val Ile Glu Val Ile Leu Pro  
                                  3125                      3130                      3135  
 Met Leu Cys Asn Tyr Leu Ser Tyr Trp Trp Glu Arg Gly Pro Glu Asn  
                                  3140                      3145                      3150  
 Leu Pro Pro Ser Thr Gly Pro Cys Cys Thr Lys Val Thr Ser Glu His  
                                  3155                      3160                      3165  
 Leu Ser Leu Ile Leu Gly Asn Ile Leu Lys Ile Ile Asn Asn Asn Leu  
                                  3170                      3175                      3180  
 Gly Ile Asp Glu Ala Ser Trp Met Lys Arg Ile Ala Val Tyr Ala Gln  
                                  3185                      3190                      3195                      3200  
 Pro Ile Ile Ser Lys Ala Arg Pro Asp Leu Leu Arg Ser His Phe Ile  
                                  3205                      3210                      3215  
 Pro Thr Leu Glu Lys Leu Lys Lys Lys Ala Val Lys Thr Val Gln Glu  
                                  3220                      3225                      3230  
 Glu Glu Gln Leu Lys Ala Asp Gly Lys Gly Asp Thr Gln Glu Ala Glu  
                                  3235                      3240                      3245  
 Leu Leu Ile Leu Asp Glu Phe Ala Val Leu Cys Arg Asp Leu Tyr Ala  
                                  3250                      3255                      3260  
 Phe Tyr Pro Met Leu Ile Arg Tyr Val Asp Asn Asn Arg Ser Asn Trp  
                                  3265                      3270                      3275                      3280

Leu Lys Ser Pro Asp Ala Asp Ser Asp Gln Leu Phe Arg Met Val Ala  
 3285 3290 3295  
 Glu Val Phe Ile Leu Trp Cys Lys Ser His Asn Phe Lys Arg Glu Glu  
 3300 3305 3310  
 Gln Asn Phe Val Ile Gln Asn Glu Ile Asn Asn Leu Ala Phe Leu Thr  
 3315 3320 3325  
 Gly Asp Ser Lys Ser Lys Met Ser Lys Ser Gly Gly Gln Asp Gln Glu  
 3330 3335 3340  
 Arg Lys Lys Thr Lys Arg Arg Gly Asp Leu Tyr Ser Ile Gln Thr Ser  
 3345 3350 3355 3360  
 Leu Ile Val Ala Ala Leu Lys Lys Met Leu Pro Ile Gly Leu Asn Met  
 3365 3370 3375  
 Cys Thr Pro Gly Asp Gln Glu Leu Ile Ser Leu Ala Lys Ser Arg Tyr  
 3380 3385 3390  
 Ser His Arg Asp Thr Asp Glu Glu Val Arg Glu His Leu Arg Asn Asn  
 3395 3400 3405  
 Leu His Leu Gln Glu Lys Ser Asp Asp Pro Ala Val Lys Trp Gln Leu  
 3410 3415 3420  
 Asn Leu Tyr Lys Asp Val Leu Lys Ser Glu Glu Pro Phe Asn Pro Glu  
 3425 3430 3435 3440  
 Lys Thr Val Glu Arg Val Gln Arg Ile Ser Ala Ala Val Phe His Leu  
 3445 3450 3455  
 Glu Gln Val Glu Gln Pro Leu Arg Ser Lys Lys Ala Val Trp His Lys  
 3460 3465 3470  
 Leu Leu Ser Lys Gln Arg Lys Arg Ala Val Val Ala Cys Phe Arg Met  
 3475 3480 3485  
 Ala Pro Leu Tyr Asn Leu Pro Arg His Arg Ser Ile Asn Leu Phe Leu  
 3490 3495 3500  
 His Gly Tyr Gln Arg Phe Trp Ile Glu Thr Glu Glu Tyr Ser Phe Glu  
 3505 3510 3515 3520  
 Glu Lys Leu Val Gln Asp Leu Ala Lys Ser Pro Lys Val Glu Glu Glu  
 3525 3530 3535  
 Glu Glu Glu Glu Thr Glu Lys Gln Pro Asp Pro Leu His Gln Ile Ile  
 3540 3545 3550  
 Leu Tyr Phe Ser Arg Asn Ala Leu Thr Glu Arg Ser Lys Leu Glu Asp  
 3555 3560 3565  
 Asp Pro Leu Tyr Thr Ser Tyr Ser Ser Met Met Ala Lys Ser Cys Gln  
 3570 3575 3580  
 Ser Gly Glu Asp Glu Glu Glu Asp Glu Asp Lys Glu Lys Thr Phe Glu  
 3585 3590 3595 3600

3605	3610	3615
His Glu Arg Gly Ala Ala Glu Met Val Leu Gln Met Ile Ser Ala Ser		
3620	3625	3630
Lys Gly Glu Met Ser Pro Met Val Val Glu Thr Leu Lys Leu Gly Ile		
3635	3640	3645
Ala Ile Leu Asn Gly Gly Asn Ala Gly Val Gln Gln Lys Met Leu Asp		
3650	3655	3660
Tyr Leu Lys Glu Lys Lys Asp Ala Gly Phe Phe Gln Ser Leu Xaa Gly		
3665	3670	3680
Leu Met Gln Ser Cys Ser Val Leu Asp Leu Asn Ala Xaa Glu Arg Gln		
3685	3690	3695
Asn Lys Ala Glu Gly Leu Gly Met Val Thr Glu Glu Gly Thr Leu Ile		
3700	3705	3710
Val Arg Glu Arg Gly Glu Lys Val Leu Gln Asn Asp Glu Phe Thr Arg		
3715	3720	3725
Asp Leu Phe Arg Phe Leu Gln Leu Leu Cys Glu Gly His Asn Ser Asp		
3730	3735	3740
Phe Gln Asn Phe Leu Arg Thr Gln Met Gly Asn Thr Thr Thr Val Asn		
3745	3750	3760
Val Ile Ile Ser Thr Val Asp Tyr Leu Leu Arg Leu Gln Glu Ser Ile		
3765	3770	3775
Ser Asp Phe Tyr Trp Tyr Tyr Ser Gly Lys Asp Ile Ile Asp Glu Ser		
3780	3785	3790
Gly Gln His Asn Phe Ser Lys Ala Leu Ala Val Thr Lys Gln Ile Phe		
3795	3800	3805
Asn Ser Leu Thr Glu Tyr Ile Gln Gly Pro Cys Ile Gly Asn Gln Gln		
3810	3815	3820
Ser Leu Ala His Ser Arg Leu Trp Asp Ala Val Val Gly Phe Leu His		
3825	3830	3840
Val Phe Ala Asn Met Gln Met Lys Leu Ser Gln Asp Ser Ser Gln Ile		
3845	3850	3855
Glu Leu Leu Lys Glu Leu Leu Asp Leu Leu Gln Asp Met Val Val Met		
3860	3865	3870
Leu Leu Ser Leu Leu Glu Gly Asn Val Val Asn Gly Thr Ile Gly Lys		
3875	3880	3885
Gln Met Val Asp Thr Leu Val Glu Ser Ser Thr Asn Val Glu Met Ile		
3890	3895	3900
Leu Lys Phe Phe Asp Met Phe Leu Lys Leu Lys Asp Leu Thr Ser Ser		
3905	3910	3920
Asp Thr Phe Lys Glu Tyr Asp Pro Asp Gly Lys Gly Ile Ile Ser Lys		

3925	3930	3935
Lys Glu Phe Gln Lys Ala Met Glu Gly Gln Lys Gln Tyr Thr Gln Ser		
3940	3945	3950
Glu Ile Asp Phe Leu Leu Ser Cys Ala Glu Ala Asp Glu Asn Asp Met		
3955	3960	3965
Phe Asn Tyr Val Asp Phe Val Asp Arg Phe His Glu Pro Ala Lys Asp		
3970	3975	3980
Ile Gly Phe Asn Val Ala Val Leu Leu Thr Asn Leu Ser Glu His Met		
3985	3990	4000
Pro Asn Asp Ser Arg Leu Lys Cys Leu Leu Asp Pro Ala Glu Ser Val		
4005	4010	4015
Leu Asn Tyr Phe Xaa Pro Tyr Leu Gly Arg Ile Glu Ile Met Gly Gly		
4020	4025	4030
Ala Lys Lys Ile Glu Arg Val Tyr Phe Glu Ile Ser Glu Ser Ser Arg		
4035	4040	4045
Thr Gln Trp Glu Lys Pro Gln Val Lys Glu Ser Lys Arg Gln Phe Ile		
4050	4055	4060
Phe Asp Val Val Asn Glu Gly Gly Glu Gln Glu Lys Met Xaa Leu Phe		
4065	4070	4075
Val Asn Phe Cys Glu Asp Thr Ile Phe Glu Met Gln Leu Ala Ser Gln		
4085	4090	4095
Ile Ser Glu Ser Asp Ser Ala Asp Arg Pro Glu Glu Glu Glu Glu Asp		
4100	4105	4110
Glu Asp Ser Ser Tyr Val Leu Glu Ile Ala Gly Glu Glu Glu Glu Asp		
4115	4120	4125
Gly Ser Leu Glu Pro Ala Ser Ala Phe Ala Met Ala Cys Ala Ser Val		
4130	4135	4140
Lys Arg Asn Val Thr Asp Phe Leu Lys Arg Ala Thr Leu Lys Asn Leu		
4145	4150	4155
Arg Lys Gln Tyr Arg Asn Val Lys Lys Met Thr Ala Lys Glu Leu Val		
4165	4170	4175
Lys Val Leu Phe Ser Phe Phe Trp Met Leu Phe Val Gly Leu Phe Gln		
4180	4185	4190
Leu Leu Phe Thr Ile Leu Gly Gly Ile Phe Gln Ile Leu Trp Ser Thr		
4195	4200	4205
Val Phe Gly Gly Gly Leu Val Glu Gly Ala Lys Asn Ile Arg Val Thr		
4210	4215	4220
Lys Ile Leu Gly Asp Met Pro Asp Pro Thr Gln Phe Gly Ile His Asp		
4225	4230	4235
Asp Thr Met Glu Ala Glu Arg Ala Glu Val Met Glu Pro Gly Ile Thr		
4245	4250	4255

Thr Glu Leu Val His Phe Ile Lys Gly Glu Lys Gly Asp Thr Asp Ile  
 4260 4265 4270  
 Met Ser Asp Leu Phe Gly Leu His Pro Lys Lys Glu Gly Ser Leu Lys  
 4275 4280 4285  
 His Gly Pro Glu Val Gly Leu Gly Asp Leu Ser Glu Ile Ile Gly Lys  
 4290 4295 4300  
 Asp Glu Pro Pro Thr Leu Glu Ser Thr Val Gln Lys Lys Arg Lys Ala  
 4305 4310 4315 4320  
 Gln Ala Ala Glu Met Lys Ala Ala Asn Glu Ala Glu Gly Lys Val Glu  
 4325 4330 4335  
 Ser Glu Lys Ala Asp Met Glu Asp Gly Glu Lys Glu Asp Lys Asp Lys  
 4340 4345 4350  
 Glu Glu Glu Gln Ala Glu Tyr Leu Trp Thr Glu Val Thr Lys Lys Lys  
 4355 4360 4365  
 Lys Arg Arg Cys Gly Gln Lys Val Glu Lys Pro Glu Ala Phe Thr Ala  
 4370 4375 4380  
 Asn Phe Phe Lys Gly Leu Glu Ile Tyr Gln Thr Lys Leu Leu His Tyr  
 4385 4390 4395 4400  
 Leu Ala Arg Asn Phe Tyr Asn Leu Arg Phe Leu Ala Leu Phe Val Ala  
 4405 4410 4415  
 Phe Ala Ile Asn Phe Ile Leu Leu Phe Tyr Lys Val Thr Glu Glu Pro  
 4420 4425 4430  
 Leu Glu Glu Glu Thr Glu Asp Val Ala Asn Leu Trp Asn Ser Phe Asn  
 4435 4440 4445  
 Asp Glu Glu Glu Glu Glu Ala Met Val Phe Phe Val Leu Gln Glu Ser  
 4450 4455 4460  
 Thr Gly Tyr Met Ala Pro Thr Leu Arg Ala Leu Ala Ile Ile His Thr  
 4465 4470 4475 4480  
 Ile Ile Ser Leu Val Cys Val Val Gly Tyr Tyr Cys Leu Lys Val Pro  
 4485 4490 4495  
 Leu Val Val Phe Lys Arg Glu Lys Glu Ile Ala Arg Lys Leu Glu Phe  
 4500 4505 4510  
 Asp Gly Leu Tyr Ile Thr Glu Gln Pro Ser Glu Asp Asp Ile Lys Gly  
 4515 4520 4525  
 Gln Trp Asp Xaa Leu Val Ile Asn Thr Pro Ser Phe Pro Asn Asn Tyr  
 4530 4535 4540  
 Trp Asp Lys Phe Val Lys Arg Lys Val Ile Asn Lys Tyr Gly Asp Leu  
 4545 4550 4555 4560  
 Tyr Gly Ala Glu Arg Ile Ala Glu Leu Leu Gly Leu Asp Lys Asn Ala  
 4565 4570 4575



Leu Asp Phe Ser Pro Val Glu Glu Thr Lys Ala Glu Ala Ala Ser Leu  
 4580 4585 4590  
 Val Ser Trp Leu Ser Ser Xaa Asp Met Lys Tyr His Ile Trp Lys Leu  
 4595 4600 4605  
 Gly Val Val Phe Thr Asp Asn Ser Phe Leu Tyr Leu Ala Trp Tyr Thr  
 4610 4615 4620  
 Thr Met Ser Val Leu Gly His Tyr Asn Asn Phe Phe Phe Ala Ala His  
 4625 4630 4635 4640  
 Leu Leu Asp Ile Ala Met Gly Phe Lys Thr Leu Arg Thr Ile Leu Ser  
 4645 4650 4655  
 Ser Val Thr His Asn Gly Lys Gln Leu Val Leu Thr Val Gly Leu Leu  
 4660 4665 4670  
 Ala Val Val Val Tyr Leu Tyr Thr Val Val Ala Phe Asn Phe Phe Arg  
 4675 4680 4685  
 Lys Phe Tyr Asn Lys Ser Glu Asp Asp Asp Glu Pro Asp Met Lys Cys  
 4690 4695 4700  
 Asp Asp Met Met Thr Cys Tyr Leu Phe His Met Tyr Val Gly Val Arg  
 4705 4710 4715 4720  
 Ala Gly Gly Gly Ile Gly Asp Glu Ile Glu Asp Pro Ala Gly Asp Pro  
 4725 4730 4735  
 Tyr Glu Met Tyr Arg Ile Val Phe Asp Ile Thr Phe Phe Phe Phe Val  
 4740 4745 4750  
 Ile Val Ile Leu Leu Ala Ile Ile Gln Gly Leu Ile Ile Asp Ala Phe  
 4755 4760 4765  
 Gly Glu Leu Arg Asp Gln Gln Glu Gln Val Arg Glu Asp Met Glu Val  
 4770 4775 4780  
 Met Leu Leu  
 4785

<210> 127  
 <211> 374  
 <212> PRT  
 <213> Homo sapiens

<400> 127  
 Met Arg Thr Leu Leu Pro Pro Ala Leu Leu Thr Cys Trp Leu Leu Ala  
 1 5 10 15  
 Pro Val Asn Ser Ile His Pro Glu Cys Arg Phe His Leu Glu Ile Gln  
 20 25 30  
 Glu Glu Glu Thr Lys Cys Xaa Glu Leu Leu Arg Ser Gln Thr Glu Lys  
 35 40 45  
 His Lys Ala Cys Ser Gly Val Trp Asp Asn Ile Thr Cys Trp Arg Pro  
 50 55 60

Ala Asn Val Gly Glu Thr Val Thr Val Pro Cys Pro Lys Val Phe Ser  
 65 70 75 80  
 Asn Phe Tyr Ser Lys Ala Gly Asn Ile Ser Lys Asn Cys Thr Ser Asp  
 85 90 95  
 Gly Trp Ser Glu Thr Phe Pro Asp Phe Val Asp Ala Cys Gly Tyr Ser  
 100 105 110  
 Asp Pro Glu Asp Glu Ser Lys Ile Thr Phe Tyr Ile Leu Val Lys Ala  
 115 120 125  
 Ile Tyr Thr Leu Gly Tyr Ser Val Ser Leu Met Ser Leu Ala Thr Gly  
 130 135 140  
 Ser Ile Ile Leu Cys Leu Phe Arg Lys Leu His Cys Thr Arg Asn Tyr  
 145 150 155 160  
 Ile His Leu Asn Leu Phe Leu Ser Phe Ile Leu Arg Ala Ile Ser Val  
 165 170 175  
 Leu Val Lys Asp Asp Val Leu Tyr Ser Ser Ser Gly Thr Leu His Cys  
 180 185 190  
 Pro Asp Gln Pro Ser Ser Trp Val Gly Cys Lys Leu Ser Leu Val Phe  
 195 200 205  
 Leu Gln Tyr Cys Ile Met Ala Asn Phe Phe Trp Leu Leu Val Glu Gly  
 210 215 220  
 Leu Tyr Leu His Thr Leu Leu Val Ala Met Leu Pro Pro Arg Arg Cys  
 225 230 235 240  
 Phe Leu Ala Tyr Leu Leu Ile Gly Trp Gly Leu Pro Thr Val Cys Ile  
 245 250 255  
 Gly Ala Trp Thr Ala Ala Arg Leu Tyr Leu Glu Asp Thr Gly Cys Trp  
 260 265 270  
 Asp Thr Asn Asp His Ser Val Pro Trp Trp Val Ile Arg Ile Pro Ile  
 275 280 285  
 Leu Ile Ser Ile Ile Val Asn Phe Val Leu Phe Ile Ser Ile Ile Arg  
 290 295 300  
 Ile Leu Leu Gln Lys Leu Thr Ser Pro Asp Val Gly Gly Asn Asp Gln  
 305 310 315 320  
 Ser Gln Tyr Lys Arg Leu Ala Lys Ser Thr Leu Leu Leu Ile Pro Leu  
 325 330 335  
 Phe Gly Val His Tyr Met Val Phe Ala Val Phe Pro Ile Ser Ile Ser  
 340 345 350  
 Ser Lys Tyr Gln Ile Leu Phe Glu Leu Cys Leu Gly Ser Phe Gln Val  
 355 360 365  
 Gly Val Arg Arg Arg Pro  
 370

<210> 128  
 <211> 447  
 <212> PRT  
 <213> Homo sapiens

<400> 128  
 Met Ala Gly Val Val His Val Ser Leu Ala Ala Leu Leu Leu Leu Pro  
           1                          5                          10                          15  
 Met Ala Pro Ala Met His Ser Asp Cys Ile Phe Lys Lys Glu Gln Ala  
                           20                          25                          30  
 Met Cys Leu Glu Lys Ile Gln Arg Ala Asn Glu Leu Met Gly Phe Asn  
                           35                          40                          45  
 Asp Ser Ser Pro Gly Cys Pro Gly Met Trp Asp Asn Ile Thr Cys Trp  
           50                          55                          60  
 Lys Pro Ala His Val Gly Glu Met Val Leu Val Ser Cys Pro Glu Leu  
           65                          70                          75                          80  
 Phe Arg Ile Phe Asn Pro Asp Gln Asp Met Gly Val Val Ser Arg Asn  
                           85                          90                          95  
 Cys Thr Glu Asp Gly Trp Ser Glu Pro Phe Pro His Tyr Phe Asp Ala  
                           100                          105                          110  
 Cys Gly Phe Asp Glu Tyr Glu Ser Glu Thr Gly Asp Gln Asp Tyr Tyr  
           115                          120                          125  
 Tyr Leu Ser Val Lys Ala Leu Tyr Thr Val Gly Tyr Ser Thr Ser Leu  
           130                          135                          140  
 Val Thr Leu Thr Thr Ala Met Val Ile Leu Cys Arg Phe Arg Lys Leu  
           145                          150                          155                          160  
 His Cys Thr Arg Asn Phe Ile His Met Asn Leu Phe Val Ser Phe Met  
                           165                          170                          175  
 Leu Arg Ala Ile Ser Val Phe Ile Lys Asp Trp Ile Leu Tyr Ala Glu  
                           180                          185                          190  
 Gln Asp Ser Asn His Cys Phe Ile Ser Thr Val Glu Cys Lys Ala Val  
           195                          200                          205  
 Met Val Phe Phe His Tyr Cys Val Val Ser Asn Tyr Phe Trp Leu Phe  
           210                          215                          220  
 Ile Glu Gly Leu Tyr Leu Phe Thr Leu Leu Val Glu Thr Phe Phe Pro  
           225                          230                          235                          240  
 Glu Arg Arg Tyr Phe Tyr Trp Tyr Thr Ile Ile Gly Trp Gly Thr Pro  
                           245                          250                          255  
 Thr Val Cys Val Thr Val Trp Ala Thr Leu Arg Leu Tyr Phe Asp Asp  
                           260                          265                          270  
 Thr Gly Cys Trp Asp Met Asn Asp Ser Thr Ala Leu Trp Trp Val Ile  
           275                          280                          285

290                                      295                                      300  
 Gly Ile Ile Val Ile Leu Val Gln Lys Leu Gln Ser Pro Asp Met Gly  
 305                                      310                                      315                                      320  
 Gly Asn Glu Ser Ser Ile Tyr Leu Arg Leu Ala Arg Ser Thr Leu Leu  
                                     325                                      330                                      335  
 Leu Ile Pro Leu Phe Gly Ile His Tyr Thr Val Phe Ala Phe Ser Pro  
                                     340                                      345                                      350  
 Glu Asn Val Ser Lys Arg Glu Arg Leu Val Phe Glu Leu Gly Leu Gly  
                                     355                                      360                                      365  
 Ser Phe Gln Gly Phe Val Val Ala Val Leu Tyr Cys Phe Leu Asn Gly  
                                     370                                      375                                      380  
 Glu Val Gln Ala Glu Ile Lys Arg Lys Trp Arg Ser Trp Lys Val Asn  
 385                                      390                                      395                                      400  
 Arg Tyr Phe Ala Val Asp Phe Lys His Arg His Pro Ser Leu Ala Ser  
                                     405                                      410                                      415  
 Ser Gly Val Asn Gly Gly Thr Gln Leu Ser Ile Leu Ser Lys Ser Ser  
                                     420                                      425                                      430  
 Ser Gln Ile Arg Met Ser Gly Leu Pro Ala Asp Asn Leu Ala Thr  
                                     435                                      440                                      445  
  
 <210> 129  
 <211> 381  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 129  
 Met Glu Arg Gly Leu Pro Leu Leu Cys Ala Val Leu Ala Leu Val Leu  
   1                                      5                                      10                                      15  
 Ala Pro Ala Gly Ala Phe Arg Asn Asp Lys Cys Gly Asp Thr Ile Lys  
                                     20                                      25                                      30  
 Ile Glu Ser Pro Gly Tyr Leu Thr Ser Pro Gly Tyr Pro His Ser Tyr  
                                     35                                      40                                      45  
 His Pro Ser Glu Lys Cys Glu Trp Leu Ile Gln Ala Pro Asp Pro Tyr  
                                     50                                      55                                      60  
 Gln Arg Ile Met Ile Asn Phe Asn Pro His Phe Asp Leu Glu Asp Arg  
   65                                      70                                      75                                      80  
 Asp Cys Lys Tyr Asp Tyr Val Glu Val Phe Asp Gly Glu Asn Glu Asn  
                                     85                                      90                                      95  
 Gly His Phe Arg Gly Lys Phe Cys Gly Lys Ile Ala Pro Pro Pro Val  
                                     100                                      105                                      110  
 Val Ser Ser Gly Pro Phe Leu Phe Ile Lys Phe Val Ser Asp Tyr Glu  
                                     115                                      120                                      125

130                      135                      140  
 Pro Glu Cys Ser Gln Asn Tyr Thr Thr Pro Ser Gly Val Ile Lys Ser  
 145                      150                      155                      160  
 Pro Gly Phe Pro Glu Lys Tyr Pro Asn Ser Leu Glu Cys Thr Tyr Ile  
 165                      170  
 Val Phe Ala Pro Lys Met Ser Glu Ile Ile Leu Glu Phe Glu Ser Phe  
 180                      185                      190  
 Asp Leu Glu Pro Asp Ser Asn Pro Pro Gly Gly Met Phe Cys Arg Tyr  
 195                      200                      205  
 Asp Arg Leu Glu Ile Trp Asp Gly Phe Pro Asp Val Gly Pro His Ile  
 210                      215                      220  
 Gly Arg Tyr Cys Gly Gln Lys Thr Pro Gly Arg Ile Arg Ser Ser Ser  
 225                      230                      235                      240  
 Gly Ile Leu Ser Met Val Phe Tyr Thr Asp Ser Ala Ile Ala Lys Glu  
 245                      250                      255  
 Gly Phe Ser Ala Asn Tyr Ser Val Leu Gln Ser Ser Val Ser Glu Asp  
 260                      265                      270  
 Phe Lys Cys Met Glu Ala Leu Gly Met Glu Ser Gly Glu Ile His Ser  
 275                      280                      285  
 Asp Gln Ile Thr Ala Ser Ser Gln Tyr Ser Thr Asn Trp Ser Ala Glu  
 290                      295                      300  
 Arg Ser Arg Leu Asn Tyr Pro Glu Asn Gly Trp Thr Pro Gly Glu Asp  
 305                      310                      315                      320  
 Ser Tyr Arg Glu Trp Ile Gln Val Asp Leu Gly Leu Leu Arg Phe Val  
 325                      330                      335  
 Thr Ala Val Gly Thr Gln Gly Ala Ile Ser Lys Glu Thr Lys Lys Lys  
 340                      345                      350  
 Tyr Tyr Val Lys Thr Tyr Lys Ile Asp Val Ser Ser Asn Gly Glu Asp  
 355                      360                      365  
 Trp Ile Thr Ile Lys Glu Gly Asn Lys Pro Val Val Ser  
 370                      375                      380

&lt;210&gt; 130

&lt;211&gt; 339

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 130

Met Glu Arg Gly Leu Pro Leu Leu Cys Ala Val Leu Ala Leu Val Leu  
 1                      5                      10                      15

Ala Pro Ala Gly Ala Phe Arg Asn Asp Lys Cys Gly Asp Thr Ile Lys  
 20                      25                      30

35	40	45
His Pro Ser Glu Lys Cys Glu Trp Leu Ile Gln Ala Pro Asp Pro Tyr 50 55 60		
Gln Arg Ile Met Ile Asn Phe Asn Pro His Phe Asp Leu Glu Asp Arg 65 70 75 80		
Asp Cys Lys Tyr Asp Tyr Val Glu Val Phe Asp Gly Glu Asn Glu Asn 85 90 95		
Gly His Phe Arg Gly Lys Phe Cys Gly Lys Ile Ala Pro Pro Pro Val 100 105 110		
Val Ser Ser Gly Pro Phe Leu Phe Ile Lys Phe Val Ser Asp Tyr Glu 115 120 125		
Thr His Gly Ala Gly Phe Ser Ile Arg Tyr Glu Ile Phe Lys Arg Gly 130 135 140		
Pro Glu Cys Ser Gln Asn Tyr Thr Thr Pro Ser Gly Val Ile Lys Ser 145 150 155 160		
Pro Gly Phe Pro Glu Lys Tyr Pro Asn Ser Leu Glu Cys Thr Tyr Ile 165 170 175		
Val Phe Ala Pro Lys Met Ser Glu Ile Ile Leu Glu Phe Glu Ser Phe 180 185 190		
Asp Leu Glu Pro Asp Ser Asn Pro Pro Gly Gly Met Phe Cys Arg Tyr 195 200 205		
Asp Arg Leu Glu Ile Trp Asp Gly Phe Pro Asp Val Gly Pro His Ile 210 215 220		
Gly Arg Tyr Cys Gly Gln Lys Thr Pro Gly Arg Ile Arg Ser Ser Ser 225 230 235 240		
Gly Ile Leu Ser Met Val Phe Tyr Thr Asp Ser Ala Ile Ala Lys Glu 245 250 255		
Gly Phe Ser Ala Asn Tyr Ser Val Leu Gln Ser Ser Val Ser Glu Asp 260 265 270		
Phe Lys Cys Met Glu Ala Leu Gly Met Glu Ser Gly Glu Ile His Ser 275 280 285		
Asp Gln Ile Thr Ala Ser Ser Gln Tyr Ser Thr Asn Trp Ser Ala Glu 290 295 300		
Arg Ser Arg Leu Asn Tyr Pro Glu Asn Gly Trp Thr Pro Gly Glu Asp 305 310 315 320		
Ser Tyr Arg Glu Trp Ile Gln Val Cys Ser Ile Arg Ser Ser Leu Ser 325 330 335		
Arg Ile Glu		

&lt;211&gt; 1350

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 131

Met Gly Arg Val Gly Tyr Trp Thr Leu Leu Val Leu Pro Ala Leu Leu  
 1 5 10 15

Val Trp Arg Gly Pro Ala Pro Ser Ala Ala Ala Glu Lys Gly Pro Pro  
 20 25 30

Ala Leu Asn Ile Ala Val Met Leu Gly His Ser His Asp Val Thr Glu  
 35 40 45

Arg Glu Leu Arg Thr Leu Trp Gly Pro Glu Gln Ala Ala Gly Leu Pro  
 50 55 60

Leu Asp Val Asn Val Val Ala Leu Leu Met Asn Arg Thr Asp Pro Lys  
 65 70 75 80

Ser Leu Ile Thr His Val Cys Asp Leu Met Ser Gly Ala Arg Ile His  
 85 90 95

Gly Leu Val Phe Gly Asp Asp Thr Asp Gln Glu Ala Val Ala Gln Met  
 100 105 110

Leu Asp Phe Ile Ser Ser His Thr Phe Val Pro Ile Leu Gly Ile His  
 115 120 125

Gly Gly Ala Ser Met Ile Met Ala Asp Lys Asp Pro Thr Ser Thr Phe  
 130 135 140

Phe Gln Phe Gly Ala Ser Ile Gln Gln Gln Ala Thr Val Met Leu Lys  
 145 150 155 160

Ile Met Gln Asp Tyr Asp Trp His Val Phe Ser Leu Val Thr Thr Ile  
 165 170 175

Phe Pro Gly Tyr Arg Glu Phe Ile Ser Phe Val Lys Thr Thr Val Asp  
 180 185 190

Asn Ser Phe Val Gly Trp Asp Met Gln Asn Val Ile Thr Leu Asp Thr  
 195 200 205

Ser Phe Glu Asp Ala Lys Thr Gln Val Gln Leu Lys Lys Ile His Ser  
 210 215 220

Ser Val Ile Leu Leu Tyr Cys Ser Lys Asp Glu Ala Val Leu Ile Leu  
 225 230 235 240

Ser Glu Ala Arg Ser Leu Gly Leu Thr Gly Tyr Asp Phe Phe Trp Ile  
 245 250 255

Val Pro Ser Leu Val Ser Gly Asn Thr Glu Leu Ile Pro Lys Glu Phe  
 260 265 270

Pro Ser Gly Leu Ile Ser Val Ser Tyr Asp Asp Trp Asp Tyr Ser Leu  
 275 280 285

Glu Ala Arg Val Arg Asp Gly Ile Gly Ile Leu Thr Thr Ala Ala Ser

Ser Met Leu Glu Lys Phe Ser Tyr Ile Pro Glu Ala Lys Ala Ser Cys  
 305 310 315 320  
 Tyr Gly Gln Met Glu Arg Pro Glu Val Pro Met His Thr Leu His Pro  
 325 330 335  
 Phe Met Val Asn Val Thr Trp Asp Gly Lys Asp Leu Ser Phe Thr Glu  
 340 345 350  
 Glu Gly Tyr Gln Val His Pro Arg Leu Val Val Ile Val Leu Asn Lys  
 355 360 365  
 Asp Arg Glu Trp Glu Lys Val Gly Lys Trp Glu Asn His Thr Leu Ser  
 370 375 380  
 Leu Arg His Ala Val Trp Pro Arg Tyr Lys Ser Phe Ser Asp Cys Glu  
 385 390 395 400  
 Pro Asp Asp Asn His Leu Ser Ile Val Thr Leu Glu Glu Ala Pro Phe  
 405 410 415  
 Val Ile Val Glu Asp Ile Asp Pro Leu Thr Glu Thr Cys Val Arg Asn  
 420 425 430  
 Thr Val Pro Cys Arg Lys Phe Val Lys Ile Asn Asn Ser Thr Asn Glu  
 435 440 445  
 Gly Met Asn Val Lys Lys Cys Cys Lys Gly Phe Cys Ile Asp Ile Leu  
 450 455 460  
 Lys Lys Leu Ser Arg Thr Val Lys Phe Thr Tyr Asp Leu Tyr Leu Val  
 465 470 475 480  
 Thr Asn Gly Lys His Gly Lys Lys Val Asn Asn Val Trp Asn Gly Met  
 485 490 495  
 Ile Gly Glu Val Val Tyr Gln Arg Ala Val Met Ala Val Gly Ser Leu  
 500 505 510  
 Thr Ile Asn Glu Glu Arg Ser Glu Val Val Asp Phe Ser Val Pro Phe  
 515 520 525  
 Val Glu Thr Gly Ile Ser Val Met Val Ser Arg Ser Asn Gly Thr Val  
 530 535 540  
 Ser Pro Ser Ala Phe Leu Glu Pro Phe Ser Ala Ser Val Trp Val Met  
 545 550 555 560  
 Met Phe Val Met Leu Leu Ile Val Ser Ala Ile Ala Val Phe Val Phe  
 565 570 575  
 Glu Tyr Phe Ser Pro Val Gly Tyr Asn Arg Asn Leu Ala Lys Gly Lys  
 580 585 590  
 Ala Pro His Gly Pro Ser Phe Thr Ile Gly Lys Ala Ile Trp Leu Leu  
 595 600 605  
 Trp Gly Leu Val Phe Asn Asn Ser Val Pro Val Gln Asn Pro Lys Gly  
 610 615 620



Thr Thr Ser Lys Ile Met Val Ser Val Trp Ala Phe Phe Ala Val Ile  
 625 630 635 640  
 Phe Leu Ala Ser Tyr Thr Ala Asn Leu Ala Ala Phe Met Ile Gln Glu  
 645 650 655  
 Glu Phe Val Asp Gln Val Thr Gly Leu Ser Asp Lys Lys Phe Gln Arg  
 660 665 670  
 Pro His Asp Tyr Ser Pro Pro Phe Arg Phe Gly Thr Val Pro Asn Gly  
 675 680 685  
 Ser Thr Glu Arg Asn Ile Arg Asn Asn Tyr Pro Tyr Met His Gln Tyr  
 690 695 700  
 Met Thr Lys Phe Asn Gln Lys Gly Val Glu Asp Ala Leu Val Ser Leu  
 705 710 715 720  
 Lys Thr Gly Lys Leu Asp Ala Phe Ile Tyr Asp Ala Ala Val Leu Asn  
 725 730 735  
 Tyr Lys Ala Gly Arg Asp Glu Gly Cys Lys Leu Val Thr Ile Gly Ser  
 740 745 750  
 Gly Tyr Ile Phe Ala Thr Thr Gly Tyr Gly Ile Ala Leu Gln Lys Gly  
 755 760 765  
 Ser Pro Trp Lys Arg Gln Ile Asp Leu Ala Leu Leu Gln Phe Val Gly  
 770 775 780  
 Asp Gly Glu Met Glu Glu Leu Glu Thr Leu Trp Leu Thr Gly Ile Cys  
 785 790 795 800  
 His Asn Glu Lys Asn Glu Val Met Ser Ser Gln Leu Asp Ile Asp Asn  
 805 810 815  
 Met Ala Gly Val Phe Tyr Met Leu Ala Ala Ala Met Ala Leu Ser Leu  
 820 825 830  
 Ile Thr Phe Ile Trp Glu His Leu Phe Tyr Trp Lys Leu Arg Phe Cys  
 835 840 845  
 Phe Thr Gly Val Cys Ser Asp Arg Pro Gly Leu Leu Phe Ser Ile Ser  
 850 855 860  
 Arg Gly Ile Tyr Ser Cys Ile His Gly Val His Ile Glu Glu Lys Lys  
 865 870 875 880  
 Lys Ser Pro Asp Phe Asn Leu Thr Gly Ser Gln Ser Asn Met Leu Lys  
 885 890 895  
 Leu Leu Arg Ser Ala Lys Asn Ile Ser Ser Met Ser Asn Met Asn Ser  
 900 905 910  
 Ser Arg Met Asp Ser Pro Lys Arg Ala Ala Asp Phe Ile Gln Arg Gly  
 915 920 925  
 Ser Leu Ile Met Asp Met Val Ser Asp Lys Gly Asn Leu Met Tyr Ser  
 930 935 940  
 Asp Asn Arg Ser Phe Gln Gly Lys Glu Ser Ile Phe Gly Asp Asn Met

945                      950                      955                      960  
 Asn Glu Leu Gln Thr Phe Val Ala Asn Arg Gln Lys Asp Asn Leu Asn  
                                  965                      970                      975  
 Asn Tyr Val Phe Gln Gly Gln His Pro Leu Thr Leu Asn Glu Ser Asn  
                                  980                      985                      990  
 Pro Asn Thr Val Glu Val Ala Val Ser Thr Glu Ser Lys Ala Asn Ser  
                                  995                      1000                      1005  
 Arg Pro Arg Gln Leu Trp Lys Lys Ser Val Asp Ser Ile Arg Gln Asp  
                                  1010                      1015                      1020  
 Ser Leu Ser Gln Asn Pro Val Ser Gln Arg Asp Glu Ala Thr Ala Glu  
                                  1025                      1030                      1035                      1040  
 Asn Arg Thr His Ser Leu Lys Ser Pro Arg Tyr Leu Pro Glu Glu Met  
                                  1045                      1050                      1055  
 Ala His Ser Asp Ile Ser Glu Thr Ser Asn Arg Ala Thr Cys His Arg  
                                  1060                      1065                      1070  
 Glu Pro Asp Asn Ser Lys Asn His Lys Thr Lys Asp Asn Phe Lys Arg  
                                  1075                      1080                      1085  
 Ser Val Ala Ser Lys Tyr Pro Lys Asp Cys Ser Glu Val Glu Arg Thr  
                                  1090                      1095                      1100  
 Tyr Leu Lys Thr Lys Ser Ser Ser Pro Arg Asp Lys Ile Tyr Thr Ile  
                                  1105                      1110                      1115                      1120  
 Asp Gly Glu Lys Glu Pro Gly Phe His Leu Asp Pro Pro Gln Phe Val  
                                  1125                      1130                      1135  
 Glu Asn Val Thr Leu Pro Glu Asn Val Asp Phe Pro Asp Pro Tyr Gln  
                                  1140                      1145                      1150  
 Asp Pro Ser Glu Asn Phe Arg Lys Gly Asp Ser Thr Leu Pro Met Asn  
                                  1155                      1160                      1165  
 Arg Asn Pro Leu His Asn Glu Gly Leu Ser Asn Asn Asp Gln Tyr  
                                  1170                      1175                      1180  
 Lys Leu Tyr Ser Lys His Phe Thr Leu Lys Asp Lys Gly Ser Pro His  
                                  1185                      1190                      1195                      1200  
 Ser Glu Thr Ser Glu Arg Tyr Arg Gln Asn Ser Thr His Cys Arg Ser  
                                  1205                      1210                      1215  
 Cys Leu Ser Asn Met Pro Thr Tyr Ser Gly His Phe Thr Met Arg Ser  
                                  1220                      1225                      1230  
 Pro Phe Lys Cys Asp Ala Cys Leu Arg Met Gly Asn Leu Tyr Asp Ile  
                                  1235                      1240                      1245  
 Asp Glu Asp Gln Met Leu Gln Glu Thr Arg Asp Asp Gln Arg Leu Val  
                                  1250                      1255                      1260  
 Ile Gly Arg Cys Pro Ser Asp Pro Tyr Lys His Ser Leu Pro Ser Gln  
                                  1265                      1270                      1275                      1280

Ala Val Asn Asp Ser Tyr Leu Arg Ser Ser Leu Arg Ser Thr Ala Ser  
 1285 1290 1295

Tyr Cys Ser Arg Asp Ser Arg Gly His Asn Asp Val Tyr Ile Ser Glu  
 1300 1305 1310

His Val Met Pro Tyr Ala Ala Asn Lys Asn Asn Met Tyr Ser Thr Pro  
 1315 1320 1325

Arg Val Leu Asn Ser Cys Ser Asn Arg Arg Val Tyr Lys Lys Met Pro  
 1330 1335 1340

Ser Ile Glu Ser Asp Val  
 1345 1350

<210> 132  
 <211> 455  
 <212> PRT  
 <213> Homo sapiens

<400> 132

Met Arg Thr Leu Leu Pro Pro Ala Leu Leu Thr Cys Trp Leu Leu Ala  
 1 5 10 15

Pro Val Asn Ser Ile His Pro Glu Cys Arg Phe His Leu Glu Ile Gln  
 20 25 30

Glu Glu Glu Thr Lys Cys Xaa Glu Leu Leu Arg Ser Gln Thr Glu Lys  
 35 40 45

His Lys Ala Cys Ser Gly Val Trp Asp Asn Ile Thr Cys Trp Arg Pro  
 50 55 60

Ala Asn Val Gly Glu Thr Val Thr Val Pro Cys Pro Lys Val Phe Ser  
 65 70 75 80

Asn Phe Tyr Ser Lys Ala Gly Asn Ile Ser Lys Asn Cys Thr Ser Asp  
 85 90 95

Gly Trp Ser Glu Thr Phe Pro Asp Phe Val Asp Ala Cys Gly Tyr Ser  
 100 105 110

Asp Pro Glu Asp Glu Ser Lys Ile Thr Phe Tyr Ile Leu Val Lys Ala  
 115 120 125

Ile Tyr Thr Leu Gly Tyr Ser Val Ser Leu Met Ser Leu Ala Thr Gly  
 130 135 140

Ser Ile Ile Leu Cys Leu Phe Arg Lys Leu His Cys Thr Arg Asn Tyr  
 145 150 155 160

Ile His Leu Asn Leu Phe Leu Ser Phe Ile Leu Arg Ala Ile Ser Val  
 165 170 175

Leu Val Lys Asp Asp Val Leu Tyr Ser Ser Ser Gly Thr Leu His Cys  
 180 185 190

Pro Asp Gln Pro Ser Ser Trp Val Gly Cys Lys Leu Ser Leu Val Phe  
 195 200 205

Leu Gln Tyr Cys Ile Met Ala Asn Phe Phe Trp Leu Leu Val Glu Gly  
 210 215 220  
 Leu Tyr Leu His Thr Leu Leu Val Ala Met Leu Pro Pro Arg Arg Cys  
 225 230 235 240  
 Phe Leu Ala Tyr Leu Leu Ile Gly Trp Gly Leu Pro Thr Val Cys Ile  
 245 250 255  
 Gly Ala Trp Thr Ala Ala Arg Leu Tyr Leu Glu Asp Thr Gly Cys Trp  
 260 265 270  
 Asp Thr Asn Asp His Ser Val Pro Trp Trp Val Ile Arg Ile Pro Ile  
 275 280 285  
 Leu Ile Ser Ile Ile Val Asn Phe Val Leu Phe Ile Ser Ile Ile Arg  
 290 295 300  
 Ile Leu Leu Gln Lys Leu Thr Ser Pro Asp Val Gly Gly Asn Asp Gln  
 305 310 315 320  
 Ser Gln Tyr Lys Arg Leu Ala Lys Ser Thr Leu Leu Leu Ile Pro Leu  
 325 330 335  
 Phe Gly Val His Tyr Met Val Phe Ala Val Phe Pro Ile Ser Ile Ser  
 340 345 350  
 Ser Lys Tyr Gln Ile Leu Phe Glu Leu Cys Leu Gly Ser Phe Gln Gly  
 355 360 365  
 Leu Val Val Ala Val Leu Tyr Cys Phe Leu Asn Ser Glu Val Ser Ser  
 370 375 380  
 Trp Pro Pro Trp Asn Gln Ala Gln Val Leu Thr Cys Phe Leu Arg Cys  
 385 390 395 400  
 Cys Pro Ala Trp Cys Arg Ser Pro His Thr Cys Leu Ser Ser Ala Gly  
 405 410 415  
 Ser Ser Tyr Cys Pro Gly Pro His Ser Ser Val Ser Pro Ser Glu Asn  
 420 425 430  
 Pro Gln Arg His Arg Gln Thr His Ser Ser Gly Pro Ser Phe Gln Thr  
 435 440 445  
 Pro Pro Ser Phe Arg Pro Pro  
 450 455  
 <210> 133  
 <211> 452  
 <212> PRT  
 <213> Homo sapiens  
 <400> 133  
 Met Arg Thr Leu Leu Pro Pro Ala Leu Leu Thr Cys Trp Leu Leu Ala  
 1 5 10 15  
 Pro Val Asn Ser Ile His Pro Glu Cys Arg Phe His Leu Glu Ile Gln  
 20 25 30

Glu	Glu	Glu	Thr	Lys	Cys	Xaa	Glu	Leu	Leu	Arg	Ser	Gln	Thr	Glu	Lys
35						40						45			
His	Lys	Ala	Cys	Ser	Gly	Val	Trp	Asp	Asn	Ile	Thr	Cys	Trp	Arg	Pro
50						55				60					
Ala	Asn	Val	Gly	Glu	Thr	Val	Thr	Val	Pro	Cys	Pro	Lys	Val	Phe	Ser
65				70						75				80	
Asn	Phe	Tyr	Ser	Lys	Ala	Gly	Asn	Ile	Ser	Lys	Asn	Cys	Thr	Ser	Asp
			85						90						
Gly	Trp	Ser	Glu	Thr	Phe	Pro	Asp	Phe	Val	Asp	Ala	Cys	Gly	Tyr	Ser
			100				105						110		
Asp	Pro	Glu	Asp	Glu	Ser	Lys	Ile	Thr	Phe	Tyr	Ile	Leu	Val	Lys	Ala
		115				120						125			
Ile	Tyr	Thr	Leu	Gly	Tyr	Ser	Val	Ser	Leu	Met	Ser	Leu	Ala	Thr	Gly
130						135				140					
Ser	Ile	Ile	Leu	Cys	Leu	Phe	Arg	Lys	Leu	His	Cys	Thr	Arg	Asn	Tyr
145				150						155				160	
Ile	His	Leu	Asn	Leu	Phe	Leu	Ser	Phe	Ile	Leu	Arg	Ala	Ile	Ser	Val
			165						170				175		
Leu	Val	Lys	Asp	Asp	Val	Leu	Tyr	Ser	Ser	Ser	Gly	Thr	Leu	His	Cys
		180						185				190			
Pro	Asp	Gln	Pro	Ser	Ser	Trp	Val	Gly	Cys	Lys	Leu	Ser	Leu	Val	Phe
		195				200						205			
Leu	Gln	Tyr	Cys	Ile	Met	Ala	Asn	Phe	Phe	Trp	Leu	Leu	Val	Glu	Gly
210						215				220					
Leu	Tyr	Leu	His	Thr	Leu	Leu	Val	Ala	Met	Leu	Pro	Pro	Arg	Arg	Cys
225				230						235				240	
Phe	Leu	Ala	Tyr	Leu	Leu	Ile	Gly	Trp	Gly	Leu	Pro	Thr	Val	Cys	Ile
			245						250				255		
Gly	Ala	Trp	Thr	Ala	Ala	Arg	Leu	Tyr	Leu	Glu	Asp	Thr	Gly	Cys	Trp
			260				265						270		
Asp	Thr	Asn	Asp	His	Ser	Val	Pro	Trp	Trp	Val	Ile	Arg	Ile	Pro	Ile
		275				280						285			
Leu	Ile	Ser	Ile	Ile	Val	Asn	Phe	Val	Leu	Phe	Ile	Ser	Ile	Ile	Arg
290						295				300					
Ile	Leu	Leu	Gln	Lys	Leu	Thr	Ser	Pro	Asp	Val	Gly	Gly	Asn	Asp	Gln
305				310						315				320	
Ser	Gln	Tyr	Lys	Arg	Leu	Ala	Lys	Ser	Thr	Leu	Leu	Leu	Ile	Pro	Leu
			325						330				335		
Phe	Gly	Val	His	Tyr	Met	Val	Phe	Ala	Val	Phe	Pro	Ile	Ser	Ile	Ser
			340				345						350		

Ser Lys Tyr Gln Ile Leu Phe Glu Leu Cys Leu Gly Ser Phe Gln Gly  
 355 360 365  
 Leu Val Val Ala Val Leu Tyr Cys Phe Leu Asn Ser Glu Val Ser Ser  
 370 375 380  
 Trp Pro Pro Trp Asn Gln Ala Gln Val Leu Thr Cys Phe Leu Arg Cys  
 385 390 395 400  
 Cys Pro Ala Trp Cys Arg Ser Pro His Thr Cys Leu Ser Ser Ala Gly  
 405 410 415  
 Ser Ser Tyr Cys Pro Gly Pro His Ser Ser Val Ser Pro Ser Glu Asn  
 420 425 430  
 Pro Gln Arg His Arg Gln Thr His Ser Ser Gly Trp Gly Val Gly Leu  
 435 440 445  
 His Ser Val Leu  
 450

<210> 134  
 <211> 1344  
 <212> PRT  
 <213> Homo sapiens

<400> 134  
 Met Lys Ser Gly Ser Gly Gly Gly Ser Pro Thr Ser Leu Trp Gly Leu  
 1 5 10 15  
 Leu Phe Leu Ser Ala Ala Leu Ser Leu Trp Pro Thr Ser Gly Glu Ile  
 20 25 30  
 Cys Gly Pro Gly Ile Asp Ile Arg Asn Asp Tyr Gln Gln Leu Lys Arg  
 35 40 45  
 Leu Glu Asn Cys Thr Val Ile Glu Gly Tyr Leu His Ile Leu Leu Ile  
 50 55 60  
 Ser Lys Ala Glu Asp Tyr Arg Ser Tyr Arg Phe Pro Lys Leu Thr Val  
 65 70 75 80  
 Ile Thr Glu Tyr Leu Leu Leu Phe Arg Val Ala Gly Leu Glu Ser Leu  
 85 90 95  
 Gly Asp Leu Phe Pro Asn Leu Thr Val Ile Arg Gly Trp Lys Leu Phe  
 100 105 110  
 Tyr Asn Tyr Ala Leu Val Ile Phe Glu Met Thr Asn Leu Lys Asp Ile  
 115 120 125  
 Gly Leu Tyr Asn Leu Arg Asn Ile Thr Arg Gly Ala Ile Arg Ile Glu  
 130 135 140  
 Lys Asn Ala Asp Leu Cys Tyr Leu Ser Thr Val Asp Trp Ser Leu Ile  
 145 150 155 160  
 Leu Asp Ala Val Ser Asn Asn Tyr Ile Val Gly Asn Lys Pro Pro Lys  
 165 170 175

Glu Cys Gly Asp Leu Cys Pro Gly Thr Met Glu Glu Lys Pro Met Cys  
 180 185 190  
 Glu Lys Thr Thr Ile Asn Asn Glu Tyr Asn Tyr Arg Cys Trp Thr Thr  
 195 200 205  
 Asn Arg Cys Gln Lys Met Cys Pro Ser Thr Cys Gly Lys Arg Ala Cys  
 210 215 220  
 Thr Glu Asn Asn Glu Cys Cys His Pro Glu Cys Leu Gly Ser Cys Ser  
 225 230 235 240  
 Ala Pro Asp Asn Asp Thr Ala Cys Val Ala Cys Arg His Tyr Tyr Tyr  
 245 250 255  
 Ala Gly Val Cys Val Pro Ala Cys Pro Pro Asn Thr Tyr Arg Phe Glu  
 260 265 270  
 Gly Trp Arg Cys Val Asp Arg Asp Phe Cys Ala Asn Ile Leu Ser Ala  
 275 280 285  
 Glu Ser Ser Asp Ser Glu Gly Phe Val Ile His Asp Gly Glu Cys Met  
 290 295 300  
 Gln Glu Cys Pro Ser Gly Phe Ile Arg Asn Gly Ser Gln Ser Met Tyr  
 305 310 315 320  
 Cys Ile Pro Cys Glu Gly Pro Cys Pro Lys Val Cys Glu Glu Glu Lys  
 325 330 335  
 Lys Thr Lys Thr Ile Asp Ser Val Thr Ser Ala Gln Met Leu Gln Gly  
 340 345 350  
 Cys Thr Ile Phe Lys Gly Asn Leu Leu Ile Asn Ile Arg Arg Gly Asn  
 355 360 365  
 Asn Ile Ala Ser Glu Leu Glu Asn Phe Met Gly Leu Ile Glu Val Val  
 370 375 380  
 Thr Gly Tyr Val Lys Ile Arg His Ser His Ala Leu Val Ser Leu Ser  
 385 390 395 400  
 Phe Leu Lys Asn Leu Arg Leu Ile Leu Gly Glu Glu Gln Leu Glu Gly  
 405 410 415  
 Asn Tyr Ser Phe Tyr Val Leu Asp Asn Gln Asn Leu Gln Gln Leu Trp  
 420 425 430  
 Asp Trp Asp His Arg Asn Leu Thr Ile Lys Ala Gly Lys Met Tyr Phe  
 435 440 445  
 Ala Phe Asn Pro Lys Leu Cys Val Ser Glu Ile Tyr Arg Met Glu Glu  
 450 455 460  
 Val Thr Gly Thr Lys Gly Arg Gln Ser Lys Gly Asp Ile Asn Thr Arg  
 465 470 475 480  
 Asn Asn Gly Glu Arg Ala Ser Cys Glu Ser Asp Val Leu His Phe Thr  
 485 490 495  
 Ser Thr Thr Thr Ser Lys Asn Arg Ile Ile Ile Thr Trp His Arg Tyr

500	505	510
Arg Pro Pro Asp Tyr Arg Asp Leu Ile Ser Phe Thr Val Tyr Tyr Lys		
515	520	525
Glu Ala Pro Phe Lys Asn Val Thr Glu Tyr Asp Gly Gln Asp Ala Cys		
530	535	540
Gly Ser Asn Ser Trp Asn Met Val Asp Val Asp Leu Pro Pro Asn Lys		
545	550	555
560		
Asp Val Glu Pro Gly Ile Leu Leu His Gly Leu Lys Pro Trp Thr Gln		
565	570	575
Tyr Ala Val Tyr Val Lys Ala Val Thr Leu Thr Met Val Glu Asn Asp		
580	585	590
His Ile Arg Gly Ala Lys Ser Glu Ile Leu Tyr Ile Arg Thr Asn Ala		
595	600	605
Ser Val Pro Ser Ile Pro Leu Asp Val Leu Ser Ala Ser Asn Ser Ser		
610	615	620
Ser Gln Leu Ile Val Lys Trp Asn Pro Pro Ser Leu Pro Asn Gly Asn		
625	630	635
640		
Leu Ser Tyr Tyr Ile Val Arg Trp Gln Arg Gln Pro Gln Asp Gly Tyr		
645	650	655
Leu Tyr Arg His Asn Tyr Cys Ser Lys Asp Lys Ile Pro Ile Arg Lys		
660	665	670
Tyr Ala Asp Gly Thr Ile Asp Ile Glu Glu Val Thr Glu Asn Pro Lys		
675	680	685
Thr Glu Val Cys Gly Gly Glu Lys Gly Pro Cys Cys Ala Cys Pro Lys		
690	695	700
Thr Glu Ala Glu Lys Gln Ala Glu Lys Glu Glu Ala Glu Tyr Arg Lys		
705	710	715
720		
Val Phe Glu Asn Phe Leu His Asn Ser Ile Phe Val Pro Arg Pro Glu		
725	730	735
Arg Lys Arg Arg Asp Val Met Gln Val Ala Asn Thr Thr Met Ser Ser		
740	745	750
Arg Ser Arg Asn Thr Thr Ala Ala Asp Thr Tyr Asn Ile Thr Asp Pro		
755	760	765
Glu Glu Leu Glu Thr Glu Tyr Pro Phe Phe Glu Ser Arg Val Asp Asn		
770	775	780
Lys Glu Arg Thr Val Ile Ser Asn Leu Arg Pro Phe Thr Leu Tyr Arg		
785	790	795
800		
Ile Asp Ile His Ser Cys Asn His Glu Ala Glu Lys Leu Gly Cys Ser		
805	810	815
Ala Ser Asn Phe Val Phe Ala Arg Thr Met Pro Ala Glu Gly Ala Asp		
820	825	830



Asp Ile Pro Gly Pro Val Thr Trp Glu Pro Arg Pro Glu Asn Ser Ile  
 835 840 845  
 Phe Leu Lys Trp Pro Glu Pro Glu Asn Pro Asn Gly Leu Ile Leu Met  
 850 855 860  
 Tyr Glu Ile Lys Tyr Gly Ser Gln Val Glu Asp Gln Arg Glu Cys Val  
 865 870 875 880  
 Ser Arg Gln Glu Tyr Arg Lys Tyr Gly Gly Ala Lys Leu Asn Arg Leu  
 885 890 895  
 Asn Pro Gly Asn Tyr Thr Ala Arg Ile Gln Ala Thr Ser Leu Ser Gly  
 900 905 910  
 Asn Gly Ser Trp Thr Asp Pro Val Phe Phe Tyr Val Gln Ala Lys Thr  
 915 920 925  
 Gly Tyr Glu Asn Phe Ile His Leu Ile Ile Ala Leu Pro Val Ala Val  
 930 935 940  
 Leu Leu Ile Val Gly Gly Leu Val Ile Met Leu Tyr Val Phe His Arg  
 945 950 955 960  
 Lys Arg Asn Asn Ser Arg Leu Gly Asn Gly Val Leu Tyr Ala Ser Val  
 965 970 975  
 Asn Pro Glu Tyr Phe Ser Ala Ala Asp Val Tyr Val Pro Asp Glu Trp  
 980 985 990  
 Glu Val Ala Arg Glu Lys Ile Thr Met Ser Arg Glu Leu Gly Gln Gly  
 995 1000 1005  
 Ser Phe Gly Met Val Tyr Glu Gly Val Ala Lys Gly Val Val Lys Asp  
 1010 1015 1020  
 Glu Pro Glu Thr Arg Val Ala Ile Lys Thr Val Asn Glu Ala Ala Ser  
 1025 1030 1035 1040  
 Met Arg Glu Arg Ile Glu Phe Leu Asn Glu Ala Ser Val Met Lys Glu  
 1045 1050 1055  
 Phe Asn Cys His His Val Val Arg Leu Leu Gly Val Val Ser Gln Gly  
 1060 1065 1070  
 Gln Pro Thr Leu Val Ile Met Glu Leu Met Thr Arg Gly Asp Leu Lys  
 1075 1080 1085  
 Ser Tyr Leu Arg Ser Leu Arg Pro Glu Met Glu Asn Asn Pro Val Leu  
 1090 1095 1100  
 Ala Pro Pro Ser Leu Ser Lys Met Ile Gln Met Ala Gly Glu Ile Ala  
 1105 1110 1115 1120  
 Asp Gly Met Ala Tyr Leu Asn Ala Asn Lys Phe Val His Arg Asp Leu  
 1125 1130 1135  
 Ala Ala Arg Asn Cys Met Val Ala Glu Asp Phe Thr Val Lys Ile Gly  
 1140 1145 1150

Asp Phe Gly Met Thr Arg Asp Ile Tyr Glu Thr Asp Tyr Tyr Arg Lys  
 1155 1160 1165  
 Gly Gly Lys Gly Leu Leu Pro Val Arg Trp Met Ser Pro Glu Ser Leu  
 1170 1175 1180  
 Lys Asp Gly Val Phe Thr Thr Tyr Ser Asp Val Trp Ser Phe Gly Val  
 1185 1190 1195 1200  
 Val Leu Trp Glu Ile Ala Thr Leu Ala Glu Gln Pro Tyr Gln Gly Leu  
 1205 1210 1215  
 Ser Asn Glu Gln Val Leu Arg Phe Val Met Glu Gly Gly Leu Leu Asp  
 1220 1225 1230  
 Lys Pro Asp Asn Cys Pro Asp Met Leu Phe Glu Leu Met Arg Met Cys  
 1235 1240 1245  
 Trp Gln Tyr Asn Pro Lys Met Arg Pro Ser Phe Leu Glu Ile Ile Ser  
 1250 1255 1260  
 Ser Ile Lys Glu Glu Leu Asp Leu Glu Pro Glu Asn Met Glu Ser Val  
 1265 1270 1275 1280  
 Pro Leu Asp Pro Ser Ala Ser Ser Ser Ser Leu Pro Leu Pro Asp Arg  
 1285 1290 1295  
 His Ser Gly His Lys Ala Glu Asn Gly Pro Gly Pro Gly Val Leu Val  
 1300 1305 1310  
 Leu Arg Ala Ser Phe Asp Glu Arg Gln Pro Tyr Ala His Met Asn Gly  
 1315 1320 1325  
 Gly Arg Lys Asn Glu Arg Ala Leu Pro Leu Pro Gln Ser Ser Thr Cys  
 1330 1335 1340

<210> 135  
 <211> 600  
 <212> PRT  
 <213> Homo sapiens

<400> 135  
 Met Glu Arg Gly Leu Pro Leu Leu Cys Ala Val Leu Ala Leu Val Leu  
 1 5 10 15  
 Ala Pro Ala Gly Ala Phe Arg Asn Asp Lys Cys Gly Asp Thr Ile Lys  
 20 25 30  
 Ile Glu Ser Pro Gly Tyr Leu Thr Ser Pro Gly Tyr Pro His Ser Tyr  
 35 40 45  
 His Pro Ser Glu Lys Cys Glu Trp Leu Ile Gln Ala Pro Asp Pro Tyr  
 50 55 60  
 Gln Arg Ile Met Ile Asn Phe Asn Pro His Phe Asp Leu Glu Asp Arg  
 65 70 75 80

Asp Cys Lys Tyr Asp Tyr Val Glu Val Phe Asp Gly Glu Asn Glu Asn  
 85 90 95  
 Gly His Phe Arg Gly Lys Phe Cys Gly Lys Ile Ala Pro Pro Pro Val  
 100 105 110  
 Val Ser Ser Gly Pro Phe Leu Phe Ile Lys Phe Val Ser Asp Tyr Glu  
 115 120 125  
 Thr His Gly Ala Gly Phe Ser Ile Arg Tyr Glu Ile Phe Lys Arg Gly  
 130 135 140  
 Pro Glu Cys Ser Gln Asn Tyr Thr Thr Pro Ser Gly Val Ile Lys Ser  
 145 150 155 160  
 Pro Gly Phe Pro Glu Lys Tyr Pro Asn Ser Leu Glu Cys Thr Tyr Ile  
 165 170 175  
 Val Phe Ala Pro Lys Met Ser Glu Ile Ile Leu Glu Phe Glu Ser Phe  
 180 185 190  
 Asp Leu Glu Pro Asp Ser Asn Pro Pro Gly Gly Met Phe Cys Arg Tyr  
 195 200 205  
 Asp Arg Leu Glu Ile Trp Asp Gly Phe Pro Asp Val Gly Pro His Ile  
 210 215 220  
 Gly Arg Tyr Cys Gly Gln Lys Thr Pro Gly Arg Ile Arg Ser Ser Ser  
 225 230 235 240  
 Gly Ile Leu Ser Met Val Phe Tyr Thr Asp Ser Ala Ile Ala Lys Glu  
 245 250 255  
 Gly Phe Ser Ala Asn Tyr Ser Val Leu Gln Ser Ser Val Ser Glu Asp  
 260 265 270  
 Phe Lys Cys Met Glu Ala Leu Gly Met Glu Ser Gly Glu Ile His Ser  
 275 280 285  
 Asp Gln Ile Thr Ala Ser Ser Gln Tyr Ser Thr Asn Trp Ser Ala Glu  
 290 295 300  
 Arg Ser Arg Leu Asn Tyr Pro Glu Asn Gly Trp Thr Pro Gly Glu Asp  
 305 310 315 320  
 Ser Tyr Arg Glu Trp Ile Gln Val Asp Leu Gly Leu Leu Arg Phe Val  
 325 330 335  
 Thr Ala Val Gly Thr Gln Gly Ala Ile Ser Lys Glu Thr Lys Lys Lys  
 340 345 350  
 Tyr Tyr Val Lys Thr Tyr Lys Ile Asp Val Ser Ser Asn Gly Glu Asp  
 355 360 365  
 Trp Ile Thr Ile Lys Glu Gly Asn Lys Pro Val Leu Phe Gln Gly Asn  
 370 375 380  
 Thr Asn Pro Thr Asp Val Val Val Ala Val Phe Pro Lys Pro Leu Ile  
 385 390 395 400  
 Thr Arg Phe Val Arg Ile Lys Pro Ala Thr Trp Glu Thr Gly Ile Ser

405										410					415				
Met	Arg	Phe	Glu	Val	Tyr	Gly	Cys	Lys	Ile	Thr	Asp	Tyr	Pro	Cys	Ser				
			420					425					430						
Gly	Met	Leu	Gly	Met	Val	Ser	Gly	Leu	Ile	Ser	Asp	Ser	Gln	Ile	Thr				
		435					440					445							
Ser	Ser	Asn	Gln	Gly	Asp	Arg	Asn	Trp	Met	Pro	Glu	Asn	Ile	Arg	Leu				
	450					455					460								
Val	Thr	Ser	Arg	Ser	Gly	Trp	Ala	Leu	Pro	Pro	Ala	Pro	His	Ser	Tyr				
465					470					475					480				
Ile	Asn	Glu	Trp	Leu	Gln	Ile	Asp	Leu	Gly	Glu	Glu	Lys	Ile	Val	Arg				
				485					490					495					
Gly	Ile	Ile	Ile	Gln	Gly	Gly	Lys	His	Arg	Glu	Asn	Lys	Val	Phe	Met				
			500				505						510						
Arg	Lys	Phe	Lys	Ile	Gly	Tyr	Ser	Asn	Asn	Gly	Ser	Asp	Trp	Lys	Met				
		515					520					525							
Ile	Met	Asp	Asp	Ser	Lys	Arg	Lys	Ala	Lys	Ser	Phe	Glu	Gly	Asn	Asn				
	530					535					540								
Asn	Tyr	Asp	Thr	Pro	Glu	Leu	Arg	Thr	Phe	Pro	Ala	Leu	Ser	Thr	Arg				
545					550					555					560				
Phe	Ile	Arg	Ile	Tyr	Pro	Glu	Arg	Ala	Thr	His	Gly	Gly	Leu	Gly	Leu				
			565						570					575					
Arg	Met	Glu	Leu	Leu	Gly	Cys	Glu	Val	Glu	Ala	Pro	Thr	Ala	Gly	Pro				
			580					585					590						
Thr	Thr	Pro	Asn	Gly	Asn	Leu	Val												
		595					600												

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<210> 136
<211> 840
<212> PRT
<213> Homo sapiens
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<400> 136
Met Glu Arg Gly Leu Pro Leu Leu Cys Ala Val Leu Ala Leu Val Leu
  1             5             10             15
Ala Pro Ala Gly Ala Phe Arg Asn Asp Lys Cys Gly Asp Thr Ile Lys
          20             25             30
Ile Glu Ser Pro Gly Tyr Leu Thr Ser Pro Gly Tyr Pro His Ser Tyr
          35             40             45
His Pro Ser Glu Lys Cys Glu Trp Leu Ile Gln Ala Pro Asp Pro Tyr
          50             55             60
Gln Arg Ile Met Ile Asn Phe Asn Pro His Phe Asp Leu Glu Asp Arg
  65             70             75             80
Asp Cys Lys Tyr Asp Tyr Val Glu Val Phe Asp Gly Glu Asn Glu Asn

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				85				90				95				
Gly	His	Phe	Arg	Gly	Lys	Phe	Cys	Gly	Lys	Ile	Ala	Pro	Pro	Pro	Val	
			100				105						110			
Val	Ser	Ser	Gly	Pro	Phe	Leu	Phe	Ile	Lys	Phe	Val	Ser	Asp	Tyr	Glu	
			115				120						125			
Thr	His	Gly	Ala	Gly	Phe	Ser	Ile	Arg	Tyr	Glu	Ile	Phe	Lys	Arg	Gly	
			130				135						140			
Pro	Glu	Cys	Ser	Gln	Asn	Tyr	Thr	Thr	Pro	Ser	Gly	Val	Ile	Lys	Ser	
145						150						155			160	
Pro	Gly	Phe	Pro	Glu	Lys	Tyr	Pro	Asn	Ser	Leu	Glu	Cys	Thr	Tyr	Ile	
			165						170						175	
Val	Phe	Ala	Pro	Lys	Met	Ser	Glu	Ile	Ile	Leu	Glu	Phe	Glu	Ser	Phe	
			180						185						190	
Asp	Leu	Glu	Pro	Asp	Ser	Asn	Pro	Pro	Gly	Gly	Met	Phe	Cys	Arg	Tyr	
			195			200						205				
Asp	Arg	Leu	Glu	Ile	Trp	Asp	Gly	Phe	Pro	Asp	Val	Gly	Pro	His	Ile	
210						215						220				
Gly	Arg	Tyr	Cys	Gly	Gln	Lys	Thr	Pro	Gly	Arg	Ile	Arg	Ser	Ser	Ser	
225						230						235			240	
Gly	Ile	Leu	Ser	Met	Val	Phe	Tyr	Thr	Asp	Ser	Ala	Ile	Ala	Lys	Glu	
			245						250						255	
Gly	Phe	Ser	Ala	Asn	Tyr	Ser	Val	Leu	Gln	Ser	Ser	Val	Ser	Glu	Asp	
			260						265						270	
Phe	Lys	Cys	Met	Glu	Ala	Leu	Gly	Met	Glu	Ser	Gly	Glu	Ile	His	Ser	
			275						280						285	
Asp	Gln	Ile	Thr	Ala	Ser	Ser	Gln	Tyr	Ser	Thr	Asn	Trp	Ser	Ala	Glu	
290						295						300				
Arg	Ser	Arg	Leu	Asn	Tyr	Pro	Glu	Asn	Gly	Trp	Thr	Pro	Gly	Glu	Asp	
305						310						315			320	
Ser	Tyr	Arg	Glu	Trp	Ile	Gln	Val	Asp	Leu	Gly	Leu	Leu	Arg	Phe	Val	
			325						330						335	
Thr	Ala	Val	Gly	Thr	Gln	Gly	Ala	Ile	Ser	Lys	Glu	Thr	Lys	Lys	Lys	
			340						345						350	
Tyr	Tyr	Val	Lys	Thr	Tyr	Lys	Ile	Asp	Val	Ser	Ser	Asn	Gly	Glu	Asp	
355						360						365				
Trp	Ile	Thr	Ile	Lys	Glu	Gly	Asn	Lys	Pro	Val	Leu	Phe	Gln	Gly	Asn	
370						375						380				
Thr	Asn	Pro	Thr	Asp	Val	Val	Val	Ala	Val	Phe	Pro	Lys	Pro	Leu	Ile	
385						390						395			400	
Thr	Arg	Phe	Val	Arg	Ile	Lys	Pro	Ala	Thr	Trp	Glu	Thr	Gly	Ile	Ser	
			405						410						415	

Met Arg Phe Glu Val Tyr Gly Cys Lys Ile Thr Asp Tyr Pro Cys Ser  
 420 425 430  
 Gly Met Leu Gly Met Val Ser Gly Leu Ile Ser Asp Ser Gln Ile Thr  
 435 440 445  
 Ser Ser Asn Gln Gly Asp Arg Asn Trp Met Pro Glu Asn Ile Arg Leu  
 450 455 460  
 Val Thr Ser Arg Ser Gly Trp Ala Leu Pro Pro Ala Pro His Ser Tyr  
 465 470 475 480  
 Ile Asn Glu Trp Leu Gln Ile Asp Leu Gly Glu Glu Lys Ile Val Arg  
 485 490 495  
 Gly Ile Ile Ile Gln Gly Gly Lys His Arg Glu Asn Lys Val Phe Met  
 500 505 510  
 Arg Lys Phe Lys Ile Gly Tyr Ser Asn Asn Gly Ser Asp Trp Lys Met  
 515 520 525  
 Ile Met Asp Asp Ser Lys Arg Lys Ala Lys Gly Gly Thr Thr Val Leu  
 530 535 540  
 Ala Thr Glu Lys Pro Thr Val Ile Asp Ser Thr Ile Gln Ser Glu Phe  
 545 550 555 560  
 Pro Thr Tyr Gly Phe Asn Cys Glu Phe Gly Trp Gly Ser His Lys Thr  
 565 570 575  
 Phe Cys His Trp Glu His Asp Asn His Val Gln Leu Lys Trp Ser Val  
 580 585 590  
 Leu Thr Ser Lys Thr Gly Pro Ile Gln Asp His Thr Gly Asp Gly Asn  
 595 600 605  
 Phe Ile Tyr Ser Gln Ala Asp Glu Asn Gln Lys Gly Lys Val Ala Arg  
 610 615 620  
 Leu Val Ser Pro Val Val Tyr Ser Gln Asn Ser Ala His Cys Met Thr  
 625 630 635 640  
 Phe Trp Tyr His Met Ser Gly Ser His Val Gly Thr Leu Arg Val Lys  
 645 650 655  
 Leu Arg Tyr Gln Lys Pro Glu Glu Tyr Asp Gln Leu Val Trp Met Ala  
 660 665 670  
 Ile Gly His Gln Gly Asp His Trp Lys Glu Gly Arg Val Leu Leu His  
 675 680 685  
 Lys Ser Leu Lys Leu Tyr Gln Val Ile Phe Glu Gly Glu Ile Gly Lys  
 690 695 700  
 Gly Asn Leu Gly Gly Ile Ala Val Asp Asp Ile Ser Ile Asn Asn His  
 705 710 715 720  
 Ile Ser Gln Glu Asp Cys Ala Lys Pro Ala Asp Leu Asp Lys Lys Asn  
 725 730 735

ro Glu Ile Lys Ile Asp Glu Thr Gly Ser Thr Pro Gly Tyr Glu Gly  
                     740                                    745                                    750  
 lu Gly Glu Gly Asp Lys Asn Ile Ser Arg Lys Pro Gly Asn Val Leu  
                     755                                    760                                    765  
 ys Thr Leu Xaa Pro Ile Leu Ile Thr Ile Ile Ala Met Ser Ala Leu  
                     770                                    775                                    780  
 ly Val Leu Leu Gly Ala Val Cys Gly Val Val Leu Tyr Cys Ala Cys  
                     785                                    790                                    795                                    800  
 Trp His Asn Gly Met Ser Glu Arg Asn Leu Ser Ala Leu Glu Asn Tyr  
                                     805                                    810                                    815  
 Asn Phe Glu Leu Val Asp Gly Val Lys Leu Lys Lys Asp Lys Leu Asn  
                                     820                                    825                                    830  
 Thr Gln Ser Thr Tyr Ser Glu Ala  
                     835                                    840

<210> 137  
 <211> 538  
 <212> PRT  
 <213> Homo sapiens

<400> 137

Met Glu Arg Gly Leu Pro Leu Leu Cys Ala Val Leu Ala Leu Val Leu  
   1                                    5                                    10                                    15  
 Ala Pro Ala Gly Ala Phe Arg Asn Asp Lys Cys Gly Asp Thr Ile Lys  
                     20                                    25                                    30  
 Ile Glu Ser Pro Gly Tyr Leu Thr Ser Pro Gly Tyr Pro His Ser Tyr  
                     35                                    40                                    45  
 His Pro Ser Glu Lys Cys Glu Trp Leu Ile Gln Ala Pro Asp Pro Tyr  
                     50                                    55                                    60  
 Gln Arg Ile Met Ile Asn Phe Asn Pro His Phe Asp Leu Glu Asp Arg  
                     65                                    70                                    75                                    80  
 Asp Cys Lys Tyr Asp Tyr Val Glu Val Phe Asp Gly Glu Asn Glu Asn  
                     85                                    90                                    95  
 Gly His Phe Arg Gly Lys Phe Cys Gly Lys Ile Ala Pro Pro Pro Val  
                     100                                    105                                    110  
 Val Ser Ser Gly Pro Phe Leu Phe Ile Lys Phe Val Ser Asp Tyr Glu  
                     115                                    120                                    125  
 Thr His Gly Ala Gly Phe Ser Ile Arg Tyr Glu Ile Phe Lys Arg Gly  
                     130                                    135                                    140  
 Pro Glu Cys Ser Gln Asn Tyr Thr Thr Pro Ser Gly Val Ile Lys Ser  
                     145                                    150                                    155                                    160  
 Pro Gly Phe Pro Glu Lys Tyr Pro Asn Ser Leu Glu Cys Thr Tyr Ile  
                     165                                    170                                    175

Val Phe Ala Pro Lys Met Ser Glu Ile Ile Leu Glu Phe Glu Ser Phe  
 180 185 190  
 Asp Leu Glu Pro Asp Ser Asn Pro Pro Gly Gly Met Phe Cys Arg Tyr  
 195 200 205  
 Asp Arg Leu Glu Ile Trp Asp Gly Phe Pro Asp Val Gly Pro His Ile  
 210 215 220  
 Gly Arg Tyr Cys Gly Gln Lys Thr Pro Gly Arg Ile Arg Ser Ser Ser  
 225 230 235 240  
 Gly Ile Leu Ser Met Val Phe Tyr Thr Asp Ser Ala Ile Ala Lys Glu  
 245 250 255  
 Gly Phe Ser Ala Asn Tyr Ser Val Leu Gln Ser Ser Val Ser Glu Asp  
 260 265 270  
 Phe Lys Cys Met Glu Ala Leu Gly Met Glu Ser Gly Glu Ile His Ser  
 275 280 285  
 Asp Gln Ile Thr Ala Ser Ser Gln Tyr Ser Thr Asn Trp Ser Ala Glu  
 290 295 300  
 Arg Ser Arg Leu Asn Tyr Pro Glu Asn Gly Trp Thr Pro Gly Glu Asp  
 305 310 315 320  
 Ser Tyr Arg Glu Trp Ile Gln Val Asp Leu Gly Leu Leu Arg Phe Val  
 325 330 335  
 Thr Ala Val Gly Thr Gln Gly Ala Ile Ser Lys Glu Thr Lys Lys Lys  
 340 345 350  
 Tyr Tyr Val Lys Thr Tyr Lys Ile Asp Val Ser Ser Asn Gly Glu Asp  
 355 360 365  
 Trp Ile Thr Ile Lys Glu Gly Asn Lys Pro Val Leu Phe Gln Gly Asn  
 370 375 380  
 Thr Asn Pro Thr Asp Val Val Val Ala Val Phe Pro Lys Pro Leu Ile  
 385 390 395 400  
 Thr Arg Phe Val Arg Ile Lys Pro Ala Thr Trp Glu Thr Gly Ile Ser  
 405 410 415  
 Met Arg Phe Glu Val Tyr Gly Cys Lys Ile Thr Asp Tyr Pro Cys Ser  
 420 425 430  
 Gly Met Leu Gly Met Val Ser Gly Leu Ile Ser Asp Ser Gln Ile Thr  
 435 440 445  
 Ser Ser Asn Gln Gly Asp Arg Asn Trp Met Pro Glu Asn Ile Arg Leu  
 450 455 460  
 Val Thr Ser Arg Ser Gly Trp Ala Leu Pro Pro Ala Pro His Ser Tyr  
 465 470 475 480  
 Ile Asn Glu Trp Leu Gln Ile Asp Leu Gly Glu Glu Lys Ile Val Arg  
 485 490 495  
 Gly Ile Ile Ile Gln Gly Gly Lys His Arg Glu Asn Lys Val Phe Met



500                      505                      510  
 Arg Lys Phe Lys Ile Gly Tyr Ser Asn Asn Gly Ser Asp Trp Lys Met  
           515                      520                      525  
 Ile Met Asp Asp Ser Lys Arg Lys Ala Arg  
           530                      535  
  
 <210> 138  
 <211> 389  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 138  
 Met Gly Ala Pro Ala Cys Ala Leu Ala Leu Cys Val Ala Val Ala Ile  
       1                      5                      10                      15  
 Val Ala Gly Ala Ser Ser Glu Ser Leu Gly Thr Glu Gln Arg Val Val  
                           20                      25                      30  
 Gly Arg Ala Ala Glu Val Pro Gly Pro Glu Pro Gly Gln Gln Glu Gln  
                           35                      40                      45  
 Leu Val Phe Gly Ser Gly Asp Ala Val Glu Leu Ser Cys Pro Pro Pro  
           50                      55                      60  
 Gly Gly Gly Pro Met Gly Pro Thr Val Trp Val Lys Asp Gly Thr Gly  
       65                      70                      75                      80  
 Leu Val Pro Ser Glu Arg Val Leu Val Gly Pro Gln Arg Leu Gln Val  
                           85                      90                      95  
 Leu Asn Ala Ser His Glu Asp Ser Gly Ala Tyr Ser Cys Arg Gln Arg  
                           100                      105                      110  
 Leu Thr Gln Arg Val Leu Cys His Phe Ser Val Arg Val Thr Asp Ala  
                           115                      120                      125  
 Pro Ser Ser Gly Asp Asp Glu Asp Gly Glu Asp Glu Ala Glu Asp Thr  
           130                      135                      140  
 Gly Val Asp Thr Gly Ala Pro Tyr Trp Thr Arg Pro Glu Arg Met Asp  
       145                      150                      155                      160  
 Lys Lys Leu Leu Ala Val Pro Ala Ala Asn Thr Val Arg Phe Arg Cys  
                           165                      170                      175  
 Pro Ala Ala Gly Asn Pro Thr Pro Ser Ile Ser Trp Leu Lys Asn Gly  
                           180                      185                      190  
 Arg Glu Phe Arg Gly Glu His Arg Ile Gly Gly Ile Lys Leu Arg His  
           195                      200                      205  
 Gln Gln Trp Ser Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly  
       210                      215                      220  
 Asn Tyr Thr Cys Val Val Glu Asn Lys Phe Gly Ser Ile Arg Gln Thr  
       225                      230                      235                      240  
 Tyr Thr Leu Asp Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln



130                      135                      140  
 Ser Cys Arg Lys Glu Gln Glu Thr Cys Leu Ala Pro Glu Leu Glu His  
 145                      150                      155                      160  
 Gly Asn Tyr Ser Thr Thr Gln Arg Thr Phe Lys Val Lys Asp Ile Val  
                          165                      170                      175  
 Ala Tyr Thr Cys Thr Ala Gly Tyr Tyr Thr Thr Thr Gly Lys Gln Thr  
                          180                      185                      190  
 Gly Glu Ala Glu Cys Gln Ala Asn Gly Trp Ser Leu Thr Pro Gln Cys  
                          195                      200                      205  
 Asn Lys Leu Met Cys Ser Ser Leu Arg Leu Ile Glu Asn Gly Tyr Phe  
                          210                      215                      220  
 His Pro Val Lys Gln Thr Tyr Glu Glu Gly Asp Val Val Gln Phe Phe  
 225                      230                      235                      240  
 Cys His Glu Asn Tyr Tyr Leu Ser Gly Ser Asp Leu Ile Gln Cys Tyr  
                          245                      250                      255  
 Asn Phe Gly Trp Tyr Pro Glu Ser Pro Ile Cys Glu Gly Arg Arg Asn  
                          260                      265                      270  
 Arg Cys Pro Pro Pro Pro Val Pro Leu Asn Ser Lys Ile Gln Pro His  
                          275                      280                      285  
 Ser Thr Thr Tyr Arg His Gly Glu Arg Val His Ile Glu Cys Glu Leu  
                          290                      295                      300  
 Asn Phe Val Ile Gln Gly Ser Glu Glu Leu Leu Cys Glu Asn Gly Lys  
 305                      310                      315                      320  
 Trp Thr Glu Pro Pro Lys Cys Ile Gly Trp  
                          325                      330

<210> 140  
 <211> 1073  
 <212> PRT  
 <213> Mouse

<400> 140  
 Met Pro Trp Gly Arg Arg Pro Thr Trp Leu Leu Leu Ala Phe Leu Leu  
   1                          5                          10                          15  
 Val Phe Leu Lys Ile Ser Ile Leu Ser Val Thr Ala Trp Gln Thr Gly  
                           20                          25                          30  
 Asn Cys Gln Pro Gly Pro Leu Glu Arg Ser Glu Arg Ser Gly Thr Cys  
                           35                          40                          45  
 Ala Gly Pro Ala Pro Phe Leu Val Phe Ser Gln Gly Lys Ser Ile Ser  
                           50                          55                          60  
 Arg Ile Asp Pro Asp Gly Thr Asn His Gln Gln Leu Val Val Asp Ala  
   65                          70                          75                          80  
 Gly Ile Ser Ala Asp Met Asp Ile His Tyr Lys Lys Glu Arg Leu Tyr

158

Gly Cys Val Leu Thr Ser Asp Gly Pro Arg Cys Ile Cys Pro Ala Gly  
 420 425 430  
 Ser Val Leu Gly Arg Asp Gly Lys Thr Cys Thr Gly Cys Ser Ser Pro  
 435 440 445  
 Asp Asn Gly Gly Cys Ser Gln Ile Cys Leu Pro Leu Arg Pro Gly Ser  
 450 455 460  
 Trp Glu Cys Asp Cys Phe Pro Gly Tyr Asp Leu Gln Ser Asp Arg Lys  
 465 470 475 480  
 Ser Cys Ala Ala Ser Gly Pro Gln Pro Leu Leu Leu Phe Ala Asn Ser  
 485 490 495  
 Gln Asp Ile Arg His Met His Phe Asp Gly Thr Asp Tyr Lys Val Leu  
 500 505 510  
 Leu Ser Arg Gln Met Gly Met Val Phe Ala Leu Asp Tyr Asp Pro Val  
 515 520 525  
 Glu Ser Lys Ile Tyr Phe Ala Gln Thr Ala Leu Lys Trp Ile Glu Arg  
 530 535 540  
 Ala Asn Met Asp Gly Ser Gln Arg Glu Arg Leu Ile Thr Glu Gly Val  
 545 550 555 560  
 Asp Thr Leu Glu Gly Leu Ala Leu Asp Trp Ile Gly Arg Arg Ile Tyr  
 565 570 575  
 Trp Thr Asp Ser Gly Lys Ser Val Val Gly Gly Ser Asp Leu Ser Gly  
 580 585 590  
 Lys His His Arg Ile Ile Ile Gln Glu Arg Ile Ser Arg Pro Arg Gly  
 595 600 605  
 Ile Ala Val His Pro Arg Ala Arg Arg Leu Phe Trp Thr Asp Val Gly  
 610 615 620  
 Met Ser Pro Arg Ile Glu Ser Ala Ser Leu Gln Gly Ser Asp Arg Val  
 625 630 635 640  
 Leu Ile Ala Ser Ser Asn Leu Leu Glu Pro Ser Gly Ile Thr Ile Asp  
 645 650 655  
 Tyr Leu Thr Asp Thr Leu Tyr Trp Cys Asp Thr Lys Arg Ser Val Ile  
 660 665 670  
 Glu Met Ala Asn Leu Asp Gly Ser Lys Arg Arg Arg Leu Ile Gln Asn  
 675 680 685  
 Asp Val Gly His Pro Phe Ser Leu Ala Val Phe Glu Asp His Leu Trp  
 690 695 700  
 Val Ser Asp Trp Ala Ile Pro Ser Val Ile Arg Val Asn Lys Arg Thr  
 705 710 715 720  
 Gly Gln Asn Arg Val Arg Leu Gln Gly Ser Met Leu Lys Pro Ser Ser  
 725 730 735

Leu Val Val Val His Pro Leu Ala Lys Pro Gly Ala Asp Pro Cys Leu  
 740 745 750  
 Tyr Arg Asn Gly Gly Cys Glu His Ile Cys Gln Glu Ser Leu Gly Thr  
 755 760 765  
 Ala Arg Cys Leu Cys Arg Glu Gly Phe Val Lys Ala Trp Asp Gly Lys  
 770 775 780  
 Met Cys Leu Pro Gln Asp Tyr Pro Ile Leu Ser Gly Glu Asn Ala Asp  
 785 790 795 800  
 Leu Ser Lys Glu Val Thr Ser Leu Ser Asn Ser Thr Gln Ala Glu Val  
 805 810 815  
 Pro Asp Asp Asp Gly Thr Glu Ser Ser Thr Leu Val Ala Glu Ile Met  
 820 825 830  
 Val Ser Gly Met Asn Tyr Glu Asp Asp Cys Gly Pro Gly Gly Cys Gly  
 835 840 845  
 Ser His Ala Arg Cys Val Ser Asp Gly Glu Thr Ala Glu Cys Gln Cys  
 850 855 860  
 Leu Lys Gly Phe Ala Arg Asp Gly Asn Leu Cys Ser Asp Ile Asp Glu  
 865 870 875 880  
 Cys Val Leu Ala Arg Ser Asp Cys Pro Ser Thr Ser Ser Arg Cys Ile  
 885 890 895  
 Asn Thr Glu Gly Gly Tyr Val Cys Arg Cys Ser Glu Gly Tyr Glu Gly  
 900 905 910  
 Asp Gly Ile Ser Cys Phe Asp Ile Asp Glu Cys Gln Arg Gly Ala His  
 915 920 925  
 Asn Cys Ala Glu Asn Ala Ala Cys Thr Asn Thr Glu Gly Gly Tyr Asn  
 930 935 940  
 Cys Thr Cys Ala Gly Arg Pro Ser Ser Pro Gly Leu Ser Cys Pro Asp  
 945 950 955 960  
 Ser Thr Ala Pro Ser Leu Leu Gly Glu Asp Gly His His Leu Asp Arg  
 965 970 975  
 Asn Ser Tyr Pro Gly Cys Pro Ser Ser Tyr Asp Gly Tyr Cys Leu Asn  
 980 985 990  
 Gly Gly Val Cys Met His Ile Glu Ser Leu Asp Ser Tyr Thr Cys Asn  
 995 1000 1005  
 Cys Val Ile Gly Tyr Ser Gly Asp Arg Cys Gln Thr Pro Pro Ser Ser  
 1010 1015 1020  
 Asp Arg Gly Pro Gln Glu Ile Glu Gly Asn Ser His Leu Pro Ser Tyr  
 1025 1030 1035 1040  
 Arg Pro Val Gly Pro Glu Lys Leu His Ser Leu Gln Ser Ala Asn Gly  
 1045 1050 1055  
 Ser Cys His Glu Arg Ala Pro Asp Leu Pro Arg Gln Thr Glu Pro Val

1060

1065

1070

Gln

&lt;210&gt; 141

&lt;211&gt; 804

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 141

Met Pro Trp Gly Arg Arg Pro Thr Trp Leu Leu Leu Ala Phe Leu Leu  
 1 5 10 15

Val Phe Leu Lys Ile Ser Ile Leu Ser Val Thr Ala Trp Gln Thr Gly  
 20 25 30

Asn Cys Gln Pro Gly Pro Leu Glu Arg Ser Glu Arg Ser Gly Thr Cys  
 35 40 45

Ala Gly Pro Ala Pro Phe Leu Val Phe Ser Gln Gly Lys Ser Ile Ser  
 50 55 60

Arg Ile Asp Pro Asp Gly Thr Asn His Gln Gln Leu Val Val Asp Ala  
 65 70 75 80

Gly Ile Ser Ala Asp Met Asp Ile His Tyr Lys Lys Glu Arg Leu Tyr  
 85 90 95

Trp Val Asp Val Glu Arg Gln Val Leu Leu Arg Val Phe Leu Asn Gly  
 100 105 110

Thr Gly Leu Glu Lys Val Cys Asn Val Glu Arg Lys Val Ser Gly Leu  
 115 120 125

Ala Ile Asp Trp Ile Asp Asp Glu Val Leu Trp Val Asp Gln Gln Asn  
 130 135 140

Gly Val Ile Thr Val Thr Asp Met Thr Gly Lys Asn Ser Arg Val Leu  
 145 150 155 160

Leu Ser Ser Leu Lys His Pro Ser Asn Ile Ala Val Asp Pro Ile Glu  
 165 170 175

Arg Leu Met Phe Trp Ser Ser Glu Val Thr Gly Ser Leu His Arg Ala  
 180 185 190

His Leu Lys Gly Val Asp Val Lys Thr Leu Leu Glu Thr Gly Gly Ile  
 195 200 205

Ser Val Leu Thr Leu Asp Val Leu Asp Lys Arg Leu Phe Trp Val Gln  
 210 215 220

Asp Ser Gly Glu Gly Ser His Ala Tyr Ile His Ser Cys Asp Tyr Glu  
 225 230 235 240

Gly Gly Ser Val Arg Leu Ile Arg His Gln Ala Arg His Ser Leu Ser  
 245 250 255

Ser Met Ala Phe Phe Gly Asp Arg Ile Phe Tyr Ser Val Leu Lys Ser

162



Lys His His Arg Ile Ile Ile Gln Glu Arg Ile Ser Arg Pro Arg Gly  
 595 600 605  
 Ile Ala Val His Pro Arg Ala Arg Arg Leu Phe Trp Thr Asp Val Gly  
 610 615 620  
 Met Ser Pro Arg Ile Glu Ser Ala Ser Leu Gln Gly Ser Asp Arg Val  
 625 630 635 640  
 Leu Ile Ala Ser Ser Asn Leu Leu Glu Pro Ser Gly Ile Thr Ile Asp  
 645 650 655  
 Tyr Leu Thr Asp Thr Leu Tyr Trp Cys Asp Thr Lys Arg Ser Val Ile  
 660 665 670  
 Glu Met Ala Asn Leu Asp Gly Ser Lys Arg Arg Arg Leu Ile Gln Asn  
 675 680 685  
 Asp Val Gly His Pro Phe Ser Leu Ala Val Phe Glu Asp His Leu Trp  
 690 695 700  
 Val Ser Asp Trp Ala Ile Pro Ser Val Ile Arg Val Asn Lys Arg Thr  
 705 710 715 720  
 Gly Gln Asn Arg Val Arg Leu Gln Gly Ser Met Leu Lys Pro Ser Ser  
 725 730 735  
 Leu Val Val Val His Pro Leu Ala Lys Pro Gly Ala Asp Pro Cys Leu  
 740 745 750  
 Tyr Arg Asn Gly Gly Cys Glu His Ile Cys Gln Glu Ser Leu Gly Thr  
 755 760 765  
 Ala Arg Cys Leu Cys Arg Glu Gly Phe Val Lys Ala Trp Asp Gly Lys  
 770 775 780  
 Met Cys Leu Pro Gln Asp Tyr Pro Ile Leu Ser Gly Glu Asn Ala His  
 785 790 795 800  
 Asn Cys Ala Phe

<210> 142  
 <211> 576  
 <212> PRT  
 <213> Homo sapiens

<400> 142  
 Met Pro Trp Gly Arg Arg Pro Thr Trp Leu Leu Leu Ala Phe Leu Leu  
 1 5 10 15  
 Val Phe Leu Lys Ile Ser Ile Leu Ser Val Thr Ala Trp Gln Thr Gly  
 20 25 30  
 Asn Cys Gln Pro Gly Pro Leu Glu Arg Ser Glu Arg Ser Gly Thr Cys  
 35 40 45  
 Ala Gly Pro Ala Pro Phe Leu Val Phe Ser Gln Gly Lys Ser Ile Ser  
 50 55 60

Arg Ile Trp Ala Ile Pro Ser Val Ile Arg Val Asn Lys Arg Thr Gly  
 65 70 75 80  
 Gln Asn Arg Val Arg Leu Gln Gly Ser Met Leu Lys Pro Ser Ser Leu  
 85 90 95  
 Val Val Val His Pro Leu Ala Lys Pro Gly Ala Asp Pro Cys Leu Tyr  
 100 105 110  
 Arg Asn Gly Gly Cys Glu His Ile Cys Gln Glu Ser Leu Gly Thr Ala  
 115 120 125  
 Arg Cys Leu Cys Arg Glu Gly Phe Val Lys Ala Trp Asp Gly Lys Met  
 130 135 140  
 Cys Leu Pro Gln Asp Tyr Pro Ile Leu Ser Gly Glu Asn Ala Asp Leu  
 145 150 155 160  
 Ser Lys Glu Val Thr Ser Leu Ser Asn Ser Thr Gln Ala Glu Val Pro  
 165 170 175  
 Asp Asp Asp Gly Thr Glu Ser Ser Thr Leu Val Ala Glu Ile Met Val  
 180 185 190  
 Ser Gly Met Asn Tyr Glu Asp Asp Cys Gly Pro Gly Gly Cys Gly Ser  
 195 200 205  
 His Ala Arg Cys Val Ser Asp Gly Glu Thr Ala Glu Cys Gln Cys Leu  
 210 215 220  
 Lys Gly Phe Ala Arg Asp Gly Asn Leu Cys Ser Asp Ile Asp Glu Cys  
 225 230 235 240  
 Val Leu Ala Arg Ser Asp Cys Pro Ser Thr Ser Ser Arg Cys Ile Asn  
 245 250 255  
 Thr Glu Gly Gly Tyr Val Cys Arg Cys Ser Glu Gly Tyr Glu Gly Asp  
 260 265 270  
 Gly Ile Ser Cys Phe Asp Ile Asp Glu Cys Gln Arg Gly Ala His Asn  
 275 280 285  
 Cys Ala Glu Asn Ala Ala Cys Thr Asn Thr Glu Gly Gly Tyr Asn Cys  
 290 295 300  
 Thr Cys Ala Gly Arg Pro Ser Ser Pro Gly Leu Ser Cys Pro Asp Ser  
 305 310 315 320  
 Thr Ala Pro Ser Leu Leu Gly Glu Asp Gly His His Leu Asp Arg Asn  
 325 330 335  
 Ser Tyr Pro Gly Cys Pro Ser Ser Tyr Asp Gly Tyr Cys Leu Asn Gly  
 340 345 350  
 Gly Val Cys Met His Ile Glu Ser Leu Asp Ser Tyr Thr Cys Asn Cys  
 355 360 365  
 Val Ile Gly Tyr Ser Gly Asp Arg Cys Gln Thr Arg Asp Leu Arg Trp  
 370 375 380

Trp Glu Leu Arg His Ala Gly Tyr Gly Gln Lys His Asp Ile Met Val  
 385 390 395 400  
 Val Ala Val Cys Met Val Ala Leu Val Leu Leu Leu Leu Gly Met  
 405 410 415  
 Trp Gly Thr Tyr Tyr Tyr Arg Thr Arg Lys Gln Leu Ser Asn Pro Pro  
 420 425 430  
 Lys Asn Pro Cys Asp Glu Pro Ser Gly Ser Val Ser Ser Ser Gly Pro  
 435 440 445  
 Asp Ser Ser Ser Gly Ala Ala Val Ala Ser Cys Pro Gln Pro Trp Phe  
 450 455 460  
 Val Val Leu Glu Lys His Gln Asp Pro Lys Asn Gly Ser Leu Pro Ala  
 465 470 475 480  
 Asp Gly Thr Asn Gly Ala Val Val Asp Ala Gly Leu Ser Pro Ser Leu  
 485 490 495  
 Gln Leu Gly Ser Val His Leu Thr Ser Trp Arg Gln Lys Pro His Ile  
 500 505 510  
 Asp Gly Met Gly Thr Gly Gln Ser Cys Trp Ile Pro Pro Ser Ser Asp  
 515 520 525  
 Arg Gly Pro Gln Glu Ile Glu Gly Asn Ser His Leu Pro Ser Tyr Arg  
 530 535 540  
 Pro Val Gly Pro Glu Lys Leu His Ser Leu Gln Ser Ala Asn Gly Ser  
 545 550 555 560  
 Cys His Glu Arg Ala Pro Asp Leu Pro Arg Gln Thr Glu Pro Val Gln  
 565 570 575

<210> 143  
 <211> 376  
 <212> PRT  
 <213> Homo sapiens

<400> 143  
 Met Pro Trp Gly Arg Arg Pro Thr Trp Leu Leu Leu Ala Phe Leu Leu  
 1 5 10 15  
 Val Ser Ala Glu Cys Gln Cys Leu Lys Gly Phe Ala Arg Asp Gly Asn  
 20 25 30  
 Leu Cys Ser Asp Ile Asp Glu Cys Val Leu Ala Arg Ser Asp Cys Pro  
 35 40 45  
 Ser Thr Ser Ser Arg Cys Ile Asn Thr Glu Gly Gly Tyr Val Cys Arg  
 50 55 60  
 Cys Ser Glu Gly Tyr Glu Gly Asp Gly Ile Ser Cys Phe Asp Ile Asp  
 65 70 75 80

Glu Cys Gln Arg Gly Ala His Asn Cys Ala Glu Asn Ala Ala Cys Thr  
                                     85                                    90                                    95  
 Asn Thr Glu Gly Gly Tyr Asn Cys Thr Cys Ala Gly Arg Pro Ser Ser  
                                     100                                    105                                    110  
 Pro Gly Leu Ser Cys Pro Asp Ser Thr Ala Pro Ser Leu Leu Gly Glu  
                                     115                                    120                                    125  
 Asp Gly His His Leu Asp Arg Asn Ser Tyr Pro Gly Cys Pro Ser Ser  
                                     130                                    135                                    140  
 Tyr Asp Gly Tyr Cys Leu Asn Gly Gly Val Cys Met His Ile Glu Ser  
                                     145                                    150                                    155                                    160  
 Leu Asp Ser Tyr Thr Cys Asn Cys Val Ile Gly Tyr Ser Gly Asp Arg  
                                     165                                    170                                    175  
 Cys Gln Thr Arg Asp Leu Arg Trp Trp Glu Leu Arg His Ala Gly Tyr  
                                     180                                    185                                    190  
 Gly Gln Lys His Asp Ile Met Val Val Ala Val Cys Met Val Ala Leu  
                                     195                                    200                                    205  
 Val Leu Leu Leu Leu Leu Gly Met Trp Gly Thr Tyr Tyr Tyr Arg Thr  
                                     210                                    215                                    220  
 Arg Lys Gln Leu Ser Asn Pro Pro Lys Asn Pro Cys Asp Glu Pro Ser  
                                     225                                    230                                    235                                    240  
 Gly Ser Val Ser Ser Ser Gly Pro Asp Ser Ser Ser Gly Ala Ala Val  
                                     245                                    250                                    255  
 Ala Ser Cys Pro Gln Pro Trp Phe Val Val Leu Glu Lys His Gln Asp  
                                     260                                    265                                    270  
 Pro Lys Asn Gly Ser Leu Pro Ala Asp Gly Thr Asn Gly Ala Val Val  
                                     275                                    280                                    285  
 Asp Ala Gly Leu Ser Pro Ser Leu Gln Leu Gly Ser Val His Leu Thr  
                                     290                                    295                                    300  
 Ser Trp Arg Gln Lys Pro His Ile Asp Gly Met Gly Thr Gly Gln Ser  
                                     305                                    310                                    315                                    320  
 Cys Trp Ile Pro Pro Ser Ser Asp Arg Gly Pro Gln Glu Ile Glu Gly  
                                     325                                    330                                    335  
 Asn Ser His Leu Pro Ser Tyr Arg Pro Val Gly Pro Glu Lys Leu His  
                                     340                                    345                                    350  
 Ser Leu Gln Ser Ala Asn Gly Ser Cys His Glu Arg Ala Pro Asp Leu  
                                     355                                    360                                    365  
 Pro Arg Gln Thr Glu Pro Val Gln  
                                     370                                    375

&lt;210&gt; 144

&lt;211&gt; 1249

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 144

Met Gly Ala Ala Ser Gly Gln Arg Gly Arg Trp Pro Leu Ser Pro Pro  
 1 5 10 15  
 Leu Leu Met Leu Ser Leu Leu Val Leu Leu Leu Gln Pro Ser Pro Ala  
 20 25 30  
 Pro Ala Leu Asp Pro Gly Leu Gln Pro Gly Asn Phe Ser Pro Asp Glu  
 35 40 45  
 Ala Gly Ala Gln Leu Phe Ala Glu Ser Tyr Asn Ser Ser Ala Glu Val  
 50 55 60  
 Val Met Phe Gln Ser Thr Val Ala Ser Trp Ala His Asp Thr Asn Ile  
 65 70 75 80  
 Thr Glu Glu Asn Ala Arg Arg Gln Glu Glu Ala Ala Leu Val Ser Gln  
 85 90 95  
 Glu Phe Ala Glu Val Trp Gly Lys Lys Ala Lys Glu Leu Tyr Glu Ser  
 100 105 110  
 Ile Trp Gln Asn Phe Thr Asp Ser Lys Leu Arg Arg Ile Ile Gly Ser  
 115 120 125  
 Ile Arg Thr Leu Gly Pro Ala Asn Leu Pro Leu Ala Gln Arg Gln Gln  
 130 135 140  
 Tyr Asn Ser Leu Leu Ser Asn Met Ser Arg Ile Tyr Ser Thr Gly Lys  
 145 150 155 160  
 Val Cys Phe Pro Asn Lys Thr Ala Thr Cys Trp Ser Leu Asp Pro Glu  
 165 170 175  
 Leu Thr Asn Ile Leu Ala Ser Ser Arg Ser Tyr Ala Lys Leu Leu Phe  
 180 185 190  
 Ala Trp Glu Gly Trp His Asp Ala Val Gly Ile Pro Leu Lys Pro Leu  
 195 200 205  
 Tyr Gln Asp Phe Thr Ala Ile Ser Asn Glu Ala Tyr Arg Gln Asp Asp  
 210 215 220  
 Phe Ser Asp Thr Gly Ala Phe Trp Arg Ser Trp Tyr Glu Ser Pro Ser  
 225 230 235 240  
 Phe Glu Glu Ser Leu Glu His Ile Tyr His Gln Leu Glu Pro Leu Tyr  
 245 250 255  
 Leu Asn Leu His Ala Tyr Val Arg Arg Ala Leu His Arg Arg Tyr Gly  
 260 265 270  
 Asp Lys Tyr Val Asn Leu Arg Gly Pro Ile Pro Ala His Leu Leu Gly  
 275 280 285  
 Asp Met Trp Ala Gln Ser Trp Glu Asn Ile Tyr Asp Met Val Val Pro  
 290 295 300  
 Phe Pro Asp Lys Pro Asn Leu Asp Val Thr Ser Thr Met Val Gln Lys

305		310		315		320
Gly Trp Asn Ala Thr	His Met Phe Arg Val Ser Glu Glu Phe Phe Thr					
	325		330			335
Ser Leu Gly Leu Ser Pro Met Pro Pro Glu Phe Trp Ala Glu Ser Met						
	340		345			350
Leu Glu Lys Pro Thr Asp Gly Arg Glu Val Val Cys His Ala Ser Ala						
	355		360			365
Trp Asp Phe Tyr Asn Arg Lys Asp Phe Arg Ile Lys Gln Cys Thr Arg						
	370		375			380
Val Thr Met Glu Gln Leu Ala Thr Val His His Glu Met Gly His Val						
	385		390			395
Gln Tyr Tyr Leu Gln Tyr Lys Asp Leu His Val Ser Leu Arg Arg Gly						
	405		410			415
Ala Asn Pro Gly Phe His Glu Ala Ile Gly Asp Val Leu Ala Leu Ser						
	420		425			430
Val Ser Thr Pro Ala His Leu His Lys Ile Gly Leu Leu Asp His Val						
	435		440			445
Thr Asn Asp Ile Glu Ser Asp Ile Asn Tyr Leu Leu Lys Met Ala Leu						
	450		455			460
Glu Lys Ile Ala Phe Leu Pro Phe Gly Tyr Leu Val Asp Gln Trp Arg						
	465		470			475
Trp Gly Val Phe Ser Gly Arg Thr Pro Pro Ser Arg Tyr Asn Phe Asp						
	485		490			495
Trp Trp Tyr Leu Arg Thr Lys Tyr Gln Gly Ile Cys Pro Pro Val Ala						
	500		505			510
Arg Asn Glu Thr His Phe Asp Ala Gly Ala Lys Phe His Ile Pro Asn						
	515		520			525
Val Thr Pro Tyr Ile Arg Tyr Phe Val Ser Phe Val Leu Gln Phe Gln						
	530		535			540
Phe His Gln Ala Leu Cys Lys Glu Ala Gly His Gln Gly Pro Leu His						
	545		550			555
Gln Cys Asp Ile Tyr Gln Ser Xaa Gln Ala Gly Ala Lys Leu Lys Gln						
	565		570			575
Val Leu Gln Ala Gly Cys Ser Arg Pro Trp Gln Glu Val Leu Lys Asp						
	580		585			590
Leu Val Gly Ser Asp Ala Leu Asp Ala Lys Ala Leu Leu Glu Tyr Phe						
	595		600			605
Gln Pro Val Ser Gln Trp Leu Glu Glu Gln Asn Gln Arg Asn Gly Glu						
	610		615			620
Val Leu Gly Trp Pro Glu Asn Gln Trp Arg Pro Pro Leu Pro Asp Asn						
	625		630			635
						640

Tyr Pro Glu Gly Ile Asp Leu Glu Thr Asp Glu Ala Lys Ala Asp Arg  
 645 650 655  
 Phe Val Glu Glu Tyr Asp Arg Thr Ala Gln Val Leu Leu Asn Glu Tyr  
 660 665 670  
 Ala Glu Ala Asn Trp Gln Tyr Asn Thr Asn Ile Thr Ile Glu Gly Ser  
 675 680 685  
 Lys Ile Leu Leu Glu Lys Ser Thr Glu Val Ser Asn His Thr Leu Lys  
 690 695 700  
 Tyr Gly Thr Arg Ala Lys Thr Phe Asp Val Ser Asn Phe Gln Asn Ser  
 705 710 715 720  
 Ser Ile Lys Arg Ile Ile Lys Lys Leu Gln Asn Leu Asp Arg Ala Val  
 725 730 735  
 Leu Pro Pro Lys Glu Leu Glu Glu Tyr Asn Gln Ile Leu Leu Asp Met  
 740 745 750  
 Glu Thr Thr Tyr Ser Leu Ser Asn Ile Cys Tyr Thr Asn Gly Thr Cys  
 755 760 765  
 Met Pro Leu Glu Pro Asp Leu Thr Asn Met Met Ala Thr Ser Arg Lys  
 770 775 780  
 Tyr Glu Glu Leu Leu Trp Ala Trp Lys Ser Trp Arg Asp Lys Val Gly  
 785 790 795 800  
 Arg Ala Ile Leu Pro Phe Phe Pro Lys Tyr Val Glu Phe Ser Asn Lys  
 805 810 815  
 Ile Ala Lys Leu Asn Gly Tyr Thr Asp Ala Gly Asp Ser Trp Arg Ser  
 820 825 830  
 Leu Tyr Glu Ser Asp Asn Leu Glu Gln Asp Leu Glu Lys Leu Tyr Gln  
 835 840 845  
 Glu Leu Gln Pro Leu Tyr Leu Asn Leu His Ala Tyr Val Arg Arg Ser  
 850 855 860  
 Leu His Arg His Tyr Gly Ser Glu Tyr Ile Asn Leu Asp Gly Pro Ile  
 865 870 875 880  
 Pro Ala His Leu Leu Gly Asn Met Trp Ala Gln Thr Trp Ser Asn Ile  
 885 890 895  
 Tyr Asp Leu Val Ala Pro Phe Pro Ser Ala Pro Asn Ile Asp Ala Thr  
 900 905 910  
 Glu Ala Met Ile Lys Gln Gly Trp Thr Pro Arg Arg Ile Phe Lys Glu  
 915 920 925  
 Ala Asp Asn Phe Phe Thr Ser Leu Gly Leu Leu Pro Val Pro Pro Glu  
 930 935 940  
 Phe Trp Asn Lys Ser Met Leu Glu Lys Pro Thr Asp Gly Arg Glu Val  
 945 950 955 960

Val Cys His Pro Ser Ala Trp Asp Phe Tyr Asn Gly Lys Asp Phe Arg  
                             965                            970                            975  
 Ile Lys Gln Cys Thr Ser Val Asn Met Glu Asp Leu Val Ile Ala His  
                             980                            985                            990  
 His Glu Met Gly His Ile Gln Tyr Phe Met Gln Tyr Lys Asp Leu Pro  
                             995                            1000                            1005  
 Val Thr Phe Arg Glu Gly Ala Asn Pro Gly Phe His Glu Ala Ile Gly  
             1010                            1015                            1020  
 Asp Ile Met Ala Leu Ser Val Ser Thr Pro Lys His Leu Tyr Ser Leu  
     1025                            1030                            1035                            1040  
 Asn Leu Leu Ser Thr Glu Gly Ser Gly Tyr Glu Tyr Asp Ile Asn Phe  
                             1045                            1050                            1055  
 Leu Met Lys Met Ala Leu Asp Lys Ile Ala Phe Ile Pro Phe Ser Tyr  
                             1060                            1065                            1070  
 Leu Ile Asp Gln Trp Arg Trp Arg Val Phe Asp Gly Ser Ile Thr Lys  
             1075                            1080                            1085  
 Glu Asn Tyr Asn Gln Glu Trp Trp Ser Leu Arg Leu Lys Tyr Gln Gly  
             1090                            1095                            1100  
 Leu Cys Pro Pro Val Pro Arg Ser Gln Gly Asp Phe Asp Pro Gly Ser  
     1105                            1110                            1115                            1120  
 Lys Phe His Val Pro Ala Asn Val Pro Tyr Val Arg Tyr Phe Val Ser  
                             1125                            1130                            1135  
 Phe Ile Ile Gln Phe Gln Phe His Glu Ala Leu Cys Arg Ala Ala Gly  
                             1140                            1145                            1150  
 His Thr Gly Pro Leu His Lys Cys Asp Ile Tyr Gln Ser Lys Glu Ala  
             1155                            1160                            1165  
 Gly Lys Leu Leu Ala Asp Ala Met Lys Leu Gly Tyr Ser Lys Pro Trp  
             1170                            1175                            1180  
 Pro Glu Ala Met Lys Leu Ile Thr Gly Gln Pro Asn Met Ser Ala Ser  
     1185                            1190                            1195                            1200  
 Ala Met Met Asn Tyr Phe Lys Pro Leu Thr Glu Trp Leu Val Thr Glu  
                             1205                            1210                            1215  
 Asn Arg Arg His Gly Glu Thr Leu Gly Trp Pro Glu Tyr Asn Trp Ala  
             1220                            1225                            1230  
 Pro Asn Thr Gly Thr Thr Pro Thr Leu Pro Pro Ala Pro Gly Pro Ser  
             1235                            1240                            1245

Ser

<210> 145  
 <211> 382  
 <212> PRT



<213> Homo sapiens

<400> 145

Met	Thr	Met	Thr	Leu	His	Thr	Lys	Ala	Ser	Gly	Met	Ala	Leu	Leu	His
1				5					10					15	
Gln	Ile	Gln	Gly	Asn	Glu	Leu	Glu	Pro	Leu	Asn	Arg	Pro	Gln	Leu	Lys
			20					25					30		
Met	Pro	Met	Glu	Arg	Ala	Leu	Gly	Glu	Val	Tyr	Val	Asp	Asn	Ser	Lys
		35					40					45			
Pro	Thr	Val	Phe	Asn	Tyr	Pro	Glu	Gly	Ala	Ala	Tyr	Glu	Phe	Asn	Ala
	50					55					60				
Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ala	Ser	Ala	Pro	Val	Tyr	Gly	Gln	Ser
65				70						75					80
Gly	Ile	Ala	Tyr	Gly	Pro	Gly	Ser	Glu	Ala	Ala	Ala	Phe	Ser	Ala	Asn
				85					90						95
Ser	Leu	Gly	Ala	Phe	Pro	Gln	Leu	Asn	Ser	Val	Ser	Pro	Ser	Pro	Leu
			100					105					110		
Met	Leu	Leu	His	Pro	Pro	Pro	Gln	Leu	Ser	Pro	Phe	Leu	His	Pro	His
	115						120					125			
Gly	Gln	Gln	Val	Pro	Tyr	Tyr	Leu	Glu	Asn	Glu	Pro	Ser	Ala	Tyr	Ala
	130						135				140				
Val	Arg	Asp	Thr	Gly	Pro	Pro	Ala	Phe	Tyr	Arg	Ser	Asn	Ser	Asp	Asn
145					150					155					160
Arg	Arg	Gln	Asn	Gly	Arg	Glu	Arg	Leu	Ser	Ser	Ser	Asn	Glu	Lys	Gly
				165					170					175	
Asn	Met	Ile	Met	Glu	Ser	Ala	Lys	Glu	Thr	Arg	Tyr	Cys	Ala	Val	Cys
			180					185					190		
Asn	Asp	Tyr	Ala	Ser	Gly	Tyr	His	Tyr	Gly	Val	Trp	Ser	Cys	Glu	Gly
		195					200					205			
Cys	Lys	Ala	Phe	Phe	Lys	Arg	Ser	Ile	Gln	Gly	His	Asn	Asp	Tyr	Met
	210					215					220				
Cys	Pro	Ala	Thr	Asn	Gln	Cys	Thr	Ile	Asp	Lys	Asn	Arg	Arg	Lys	Ser
225					230					235					240
Cys	Gln	Ala	Cys	Arg	Leu	Arg	Lys	Cys	Tyr	Glu	Val	Gly	Met	Met	Lys
				245					250					255	
Gly	Gly	Ile	Arg	Lys	Asp	Arg	Arg	Gly	Gly	Arg	Met	Leu	Lys	His	Lys
			260					265					270		
Arg	Gln	Arg	Asp	Asp	Leu	Glu	Gly	Arg	Asn	Glu	Met	Gly	Ala	Ser	Gly
		275					280					285			
Asp	Met	Arg	Ala	Ala	Asn	Leu	Trp	Pro	Ser	Pro	Leu	Val	Ile	Lys	His
	290					295					300				
Thr	Lys	Lys	Asn	Ser	Pro	Ala	Leu	Ser	Leu	Thr	Ala	Asp	Gln	Met	Val

305					310						315				320
Ser	Ala	Leu	Leu	Asp	Ala	Glu	Pro	Pro	Met	Ile	Tyr	Ser	Glu	Tyr	Asp
				325					330					335	
Pro	Ser	Arg	Pro	Phe	Ser	Glu	Ala	Ser	Met	Met	Gly	Leu	Leu	Thr	Asn
			340					345					350		
Leu	Ala	Asp	Arg	Glu	Leu	Val	His	Met	Ile	Asn	Trp	Ala	Lys	Arg	Val
		355					360					365			
Pro	Gly	Lys	Asp	Ala	Lys	Leu	Asn	Phe	Tyr	Val	Lys	Ser	Glu		
	370					375					380				

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<210> 146
<211> 345
<212> PRT
<213> Homo sapiens
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<400> 146
Met Val Pro Gln Ala His Gly Leu Leu Leu Leu Cys Phe Leu Leu Gln
  1              5              10              15

Leu Gln Gly Pro Leu Gly Thr Ala Val Phe Ile Thr Gln Glu Glu Ala
      20              25              30

His Gly Val Leu His Arg Gln Arg Arg Ala Asn Ser Leu Leu Glu Glu
  35              40              45

Leu Trp Pro Gly Ser Leu Glu Arg Glu Cys Asn Glu Glu Gln Cys Ser
  50              55              60

Phe Glu Glu Ala Arg Glu Ile Phe Lys Ser Pro Glu Arg Thr Lys Gln
  65              70              75              80

Phe Trp Ile Val Tyr Ser Asp Gly Asp Gln Cys Ala Ser Asn Pro Cys
      85              90              95

Gln Asn Gly Gly Thr Cys Gln Asp His Leu Lys Ser Tyr Val Cys Phe
      100              105              110

Cys Leu Leu Asp Phe Glu Gly Ala Val Leu Leu Asp Ala Arg Trp Ile
      115              120              125

Val Thr Ala Ala His Cys Phe Asp Asn Ile Arg Tyr Trp Gly Asn Ile
      130              135              140

Thr Val Val Met Gly Glu His Asp Phe Ser Glu Lys Asp Gly Asp Glu
  145              150              155              160

Gln Val Arg Arg Val Thr Gln Val Ile Met Pro Asp Lys Tyr Ile Arg
      165              170              175

Gly Lys Ile Asn His Asp Ile Ala Leu Leu Arg Leu His Arg Pro Val
      180              185              190

Thr Phe Thr Asp Tyr Val Val Pro Leu Cys Leu Pro Glu Lys Ser Phe
      195              200              205

Ser Glu Asn Thr Leu Ala Arg Ile Arg Phe Ser Arg Val Ser Gly Trp

```

210                                      215                                      220  
 Gly Gln Leu Leu Asp Arg Gly Ala Thr Ala Leu Glu Leu Met Ser Ile  
 225                                      230                                      235                                      240  
 Glu Val Pro Arg Leu Met Thr Gln Asp Cys Leu Glu His Ala Lys His  
                                     245                                      250                                      255  
 Ser Ser Asn Thr Pro Lys Ile Thr Glu Asn Met Phe Cys Ala Gly Tyr  
                                     260                                      265                                      270  
 Met Asp Gly Thr Lys Asp Ala Cys Lys Gly Asp Ser Gly Gly Pro His  
                                     275                                      280                                      285  
 Ala Thr His Tyr His Gly Thr Trp Tyr Leu Thr Gly Val Val Ser Trp  
                                     290                                      295                                      300  
 Gly Glu Gly Cys Ala Ala Ile Gly His Ile Gly Val Tyr Thr Arg Val  
 305                                      310                                      315                                      320  
 Ser Gln Tyr Ile Asp Trp Leu Val Arg His Met Asp Ser Lys Leu Gln  
                                     325                                      330                                      335  
 Val Gly Val Phe Arg Leu Pro Leu Leu  
                                     340                                      345

<210> 147  
 <211> 103  
 <212> PRT  
 <213> Homo sapiens

<400> 147  
 Met Gly Phe Leu Lys Phe Ser Pro Phe Leu Val Val Ser Ile Leu Leu  
   1                                      5                                      10                                      15  
 Leu Ala Leu Val Gln Asp Tyr Met Gln Met Lys Ala Arg Glu Leu Glu  
                                     20                                      25                                      30  
 Gln Glu Glu Glu Gln Glu Ala Glu Gly Ser Ser Leu Asp Ser Pro Arg  
                                     35                                      40                                      45  
 Ser Lys Arg Cys Gly Asn Leu Ser Thr Cys Met Leu Gly Thr Tyr Thr  
                                     50                                      55                                      60  
 Gln Asp Leu Asn Lys Phe His Thr Phe Pro Gln Thr Ser Ile Gly Val  
                                     65                                      70                                      75                                      80  
 Glu Ala Pro Gly Lys Lys Arg Asp Val Ala Lys Asp Leu Glu Thr Asn  
                                     85                                      90                                      95  
 His Gln Ser His Phe Gly Asn  
                                     100

<210> 148  
 <211> 525  
 <212> PRT  
 <213> Homo sapiens

<400> 148

Met Ala Thr Leu Leu Arg Ser Lys Leu Thr Asn Val Ala Thr Ser Val  
 1 5 10 15  
 Ser Asn Lys Ser Gln Ala Lys Val Ser Gly Met Phe Ala Arg Met Gly  
 20 25 30  
 Phe Gln Ala Ala Thr Asp Glu Glu Ala Val Gly Phe Ala His Cys Asp  
 35 40 45  
 Asp Leu Asp Phe Glu His Arg Gln Gly Leu Gln Met Asp Ile Leu Lys  
 50 55 60  
 Ser Glu Gly Glu Pro Cys Gly Asp Glu Gly Ala Glu Ala Pro Val Glu  
 65 70 75 80  
 Gly Asp Ile His Tyr Gln Arg Gly Gly Ala Pro Leu Pro Pro Ser Gly  
 85 90 95  
 Ser Lys Asp Gln Ala Val Gly Ala Gly Gly Glu Phe Gly Gly His Asp  
 100 105 110  
 Lys Pro Lys Ile Thr Ala Trp Glu Ala Gly Trp Asn Val Thr Asn Ala  
 115 120 125  
 Ile Gln Gly Met Phe Val Leu Gly Leu Pro Tyr Ala Ile Leu His Gly  
 130 135 140  
 Gly Tyr Leu Gly Leu Phe Leu Ile Ile Phe Ala Ala Val Val Cys Cys  
 145 150 155 160  
 Tyr Thr Gly Lys Ile Leu Ile Ala Cys Leu Tyr Glu Glu Asn Glu Asp  
 165 170 175  
 Gly Glu Val Val Arg Val Arg Asp Ser Tyr Val Ala Ile Ala Asn Ala  
 180 185 190  
 Cys Cys Ala Pro Arg Phe Pro Thr Leu Gly Gly Arg Val Val Asn Val  
 195 200 205  
 Ala Gln Ile Ile Glu Leu Val Met Thr Cys Ile Leu Tyr Val Val Val  
 210 215 220  
 Ser Gly Asn Leu Met Tyr Asn Ser Phe Pro Gly Leu Pro Val Ser Gln  
 225 230 235 240  
 Lys Ser Trp Ser Ile Ile Ala Thr Ala Val Leu Leu Pro Cys Ala Phe  
 245 250 255  
 Leu Lys Asn Leu Lys Ala Val Ser Lys Phe Ser Leu Leu Cys Thr Leu  
 260 265 270  
 Ala His Phe Val Ile Asn Ile Leu Val Ile Ala Tyr Cys Leu Ser Arg  
 275 280 285  
 Ala Arg Asp Trp Ala Trp Glu Lys Val Lys Phe Tyr Ile Asp Val Lys  
 290 295 300  
 Lys Phe Pro Ile Ser Ile Gly Ile Ile Val Phe Ser Tyr Thr Ser Gln  
 305 310 315 320  
 Ile Phe Leu Pro Ser Leu Glu Gly Asn Met Gln Gln Pro Ser Glu Phe



85					90					95					
Glu	Lys	Ser	Cys	Asp	Phe	Leu	Ser	Ser	Phe	Arg	Asp	Ser	Cys	Gln	Lys
			100				105						110		
Phe	Tyr	Gln	Ala	Glu	Met	Glu	Glu	Leu	Asp	Phe	Ile	Ser	Ala	Val	Glu
			115				120						125		
Lys	Ser	Arg	Lys	His	Ile	Asn	Thr	Trp	Val	Ala	Glu	Lys	Thr	Glu	Gly
			130				135						140		
Lys	Ile	Ala	Glu	Leu	Leu	Ser	Pro	Gly	Ser	Val	Asp	Pro	Leu	Thr	Arg
			145				150						155		
Leu	Val	Leu	Val	Asn	Ala	Val	Tyr	Phe	Arg	Gly	Asn	Trp	Asp	Glu	Gln
			165				170						175		
Phe	Asp	Lys	Glu	Asn	Thr	Glu	Glu	Arg	Leu	Phe	Lys	Val	Ser	Lys	Asn
			180				185						190		
Glu	Glu	Lys	Pro	Val	Gln	Met	Met	Phe	Lys	Gln	Ser	Thr	Phe	Lys	Lys
			195				200						205		
Thr	Tyr	Ile	Gly	Glu	Ile	Phe	Thr	Gln	Ile	Leu	Val	Leu	Pro	Tyr	Val
			210				215						220		
Gly	Lys	Glu	Leu	Asn	Met	Ile	Ile	Met	Leu	Pro	Asp	Glu	Thr	Thr	Asp
			225				230						235		
Leu	Arg	Thr	Val	Glu	Lys	Glu	Leu	Thr	Tyr	Glu	Lys	Phe	Val	Glu	Trp
			245				250						255		
Thr	Arg	Leu	Asp	Met	Met	Asp	Glu	Glu	Glu	Val	Glu	Val	Ser	Leu	Pro
			260				265						270		
Arg	Phe	Lys	Leu	Glu	Glu	Ser	Tyr	Asp	Met	Glu	Ser	Val	Leu	Arg	Asn
			275				280						285		
Leu	Gly	Met	Thr	Asp	Ala	Phe	Glu	Leu	Gly	Lys	Ala	Asp	Phe	Ser	Gly
			290				295						300		
Met	Ser	Gln	Thr	Asp	Leu	Ser	Leu	Ser	Lys	Val	Val	His	Lys	Ser	Phe
			305				310						315		
Val	Glu	Val	Asn	Glu	Glu	Gly	Thr	Glu	Ala	Ala	Ala	Ala	Thr	Ala	Ala
			325				330						335		
Ile	Met	Met	Met	Arg	Cys	Ala	Arg	Phe	Val	Pro	Arg	Phe	Cys	Ala	Asp
			340				345						350		
His	Pro	Phe	Leu	Phe	Phe	Ile	Gln	His	Ser	Lys	Thr	Asn	Gly	Ile	Leu
			355				360						365		
Phe	Cys	Gly	Arg	Gln	Leu	Met	Asn	Phe	Ser	Pro	Asp	Ser	Ser	Ala	Gly
			370				375						380		
Cys	Cys	Asn	Val	Xaa	Leu	Phe	Pro	Ser	Pro	Trp	Gly	Gly	Gly	Gly	Gly
			385				390						395		
													400		

<210> 150  
 <211> 372  
 <212> PRT  
 <213> Homo sapiens

<400> 150  
 Met Asp Val Leu Ala Glu Ala Asn Gly Thr Phe Ala Leu Asn Leu Leu  
     1                    5                    10                    15  
 Lys Thr Leu Gly Lys Asp Asn Ser Lys Asn Val Phe Phe Ser Pro Met  
             20                    25                    30  
 Ser Met Ser Cys Ala Leu Ala Met Val Tyr Met Gly Ala Lys Gly Asn  
         35                    40                    45  
 Thr Ala Ala Gln Met Ala Gln Ile Leu Ser Phe Asn Lys Ser Gly Gly  
     50                    55                    60  
 Gly Gly Asp Ile His Gln Gly Phe Gln Ser Leu Leu Thr Glu Val Asn  
     65                    70                    75                    80  
 Lys Thr Gly Thr Gln Tyr Leu Leu Arg Val Ala Asn Arg Leu Phe Gly  
             85                    90                    95  
 Glu Lys Ser Cys Asp Phe Leu Ser Ser Phe Arg Asp Ser Cys Gln Lys  
         100                    105                    110  
 Phe Tyr Gln Ala Glu Met Glu Glu Leu Asp Phe Ile Ser Ala Val Glu  
     115                    120                    125  
 Lys Ser Arg Lys His Ile Asn Thr Trp Val Ala Glu Lys Thr Glu Gly  
     130                    135                    140  
 Lys Ile Ala Glu Leu Leu Ser Pro Gly Ser Val Asp Pro Leu Thr Arg  
     145                    150                    155                    160  
 Leu Val Leu Val Asn Ala Val Tyr Phe Arg Gly Asn Trp Asp Glu Gln  
             165                    170                    175  
 Phe Asp Lys Glu Asn Thr Glu Glu Arg Leu Phe Lys Val Ser Lys Asn  
     180                    185                    190  
 Glu Glu Lys Pro Val Gln Met Met Phe Lys Gln Ser Thr Phe Lys Lys  
     195                    200                    205  
 Thr Tyr Ile Gly Glu Ile Phe Thr Gln Ile Leu Val Leu Pro Tyr Val  
     210                    215                    220  
 Gly Lys Glu Leu Asn Met Ile Ile Met Leu Pro Asp Glu Thr Thr Asp  
     225                    230                    235                    240  
 Leu Arg Thr Val Glu Lys Glu Leu Thr Tyr Glu Lys Phe Val Glu Trp  
             245                    250                    255  
 Thr Arg Leu Asp Met Met Asp Glu Glu Glu Val Glu Val Ser Leu Pro  
     260                    265                    270  
 Arg Phe Lys Leu Glu Glu Ser Tyr Asp Met Glu Ser Val Leu Arg Asn  
     275                    280                    285

Leu Gly Met Thr Asp Ala Phe Glu Leu Gly Lys Ala Asp Phe Ser Gly  
 290 295 300  
 Met Ser Gln Thr Asp Leu Ser Leu Ser Lys Val Val His Lys Ser Phe  
 305 310 315 320  
 Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala Ala Thr Ala Ala  
 325 330 335  
 Ile Met Met Met Arg Cys Ala Arg Phe Val Pro Arg Phe Cys Ala Asp  
 340 345 350  
 His Pro Phe Leu Phe Phe Ile Gln Gln Arg Ile Pro Leu Val Leu Leu  
 355 360 365  
 Cys Trp Ser Thr  
 370

<210> 151  
 <211> 560  
 <212> PRT  
 <213> Homo sapiens

<400> 151  
 Met Phe Pro Asp Leu Val Gln Leu Ile Cys Ala Tyr Cys His Thr Arg  
 1 5 10 15  
 Asp Ile Leu Leu Leu Pro Leu Gln Leu Pro Arg Ala Ile His His Ala  
 20 25 30  
 Ala Thr His Lys Glu Leu Glu Ala Ile Ser His Leu Gly Ile Glu Phe  
 35 40 45  
 Trp Ser Ser Ser Leu Asn Ile Lys Ala Gln Arg Gly Pro Ala Gly Gly  
 50 55 60  
 Pro Val Leu Pro Gln Leu Lys Ala Arg Ser Pro Gln Glu Leu Asp Gln  
 65 70 75 80  
 Gly Thr Gly Ala Ala Leu Cys Phe Phe Asn Pro Leu Phe Pro Gly Asp  
 85 90 95  
 Leu Gly Pro Thr Lys Arg Glu Lys Phe Lys Arg Ser Phe Lys Val Arg  
 100 105 110  
 Val Ser Thr Glu Thr Ser Ser Pro Leu Ser Pro Pro Ala Val Pro Pro  
 115 120 125  
 Pro Pro Val Pro Val Leu Pro Gly Ala Val Pro Ser Gln Thr Glu Arg  
 130 135 140  
 Leu Pro Pro Cys Gln Leu Leu Arg Arg Glu Ser Ser Val Gly Tyr Arg  
 145 150 155 160  
 Val Pro Ala Gly Ser Gly Pro Ser Leu Pro Pro Met Pro Ser Leu Gln  
 165 170 175  
 Glu Val Asp Cys Gly Ser Pro Ser Ser Ser Glu Glu Glu Gly Val Pro  
 180 185 190



Gly Ser Arg Gly Ser Pro Ala Thr Ser Pro His Leu Gly Arg Arg Arg  
 195 200 205  
 Pro Leu Leu Arg Ser Met Ser Ala Ala Phe Cys Ser Leu Leu Ala Pro  
 210 215 220  
 Glu Arg Gln Val Gly Arg Ala Ala Ala Leu Met Gln Asp Arg His  
 225 230 235 240  
 Thr Ala Ala Gly Gln Leu Val Gln Asp Leu Leu Thr Gln Val Arg Asp  
 245 250 255  
 Gly Gln Arg Pro Gln Glu Leu Glu Gly Ile Arg Gln Ala Leu Ser Arg  
 260 265 270  
 Ala Arg Ala Met Leu Ser Ala Glu Leu Gly Pro Glu Lys Leu Val Ser  
 275 280 285  
 Pro Lys Arg Leu Glu His Val Leu Glu Lys Ser Leu His Cys Ser Val  
 290 295 300  
 Leu Lys Pro Leu Arg Pro Ile Leu Ala Ala Arg Leu Arg Arg Arg Leu  
 305 310 315 320  
 Ala Ala Asp Gly Ser Leu Gly Arg Leu Ala Glu Gly Leu Arg Leu Ala  
 325 330 335  
 Arg Ala Gln Gly Pro Gly Ala Phe Gly Ser His Leu Ser Leu Pro Ser  
 340 345 350  
 Pro Val Glu Leu Glu Gln Val Arg Gln Lys Leu Leu Gln Leu Val Arg  
 355 360 365  
 Thr Tyr Ser Pro Ser Ala Gln Val Lys Arg Leu Leu Gln Ala Cys Lys  
 370 375 380  
 Leu Leu Tyr Met Ala Leu Arg Thr Gln Glu Gly Glu Gly Ser Gly Ala  
 385 390 395 400  
 Asp Gly Phe Leu Pro Leu Leu Ser Leu Val Leu Ala His Cys Asp Leu  
 405 410 415  
 Pro Glu Leu Leu Leu Glu Ala Glu Tyr Met Ser Glu Leu Leu Glu Pro  
 420 425 430  
 Ser Leu Leu Thr Gly Glu Gly Gly Tyr Tyr Leu Thr Ser Leu Ser Ala  
 435 440 445  
 Ser Leu Ala Leu Leu Ser Gly Leu Gly Gln Ala His Thr Leu Pro Leu  
 450 455 460  
 Ser Pro Val Gln Glu Leu Arg Arg Ser Leu Ser Leu Trp Glu Gln Arg  
 465 470 475 480  
 Arg Leu Pro Ala Thr His Cys Phe Gln Val Thr Gly Pro Pro Pro Cys  
 485 490 495  
 Pro Gln Ser Gln Thr Pro Ser Pro Pro Xaa Thr Phe Leu Ser Leu Val  
 500 505 510

Lys Ser Pro Asp Ser Val Asp Arg Ser Trp Val Leu Ile Leu Ala Leu  
 515 520 525

His Trp Val Val Gly Thr Trp Ala Ser Tyr Leu Thr Thr Ser Cys Leu  
 530 535 540

Ser Phe Leu Ile Ser Lys Met Gly Val Ile Gly Pro Thr Ser Trp Gly  
 545 550 555 560

<210> 152  
 <211> 437  
 <212> PRT  
 <213> Homo sapiens

<400> 152

Met Leu Ile Ala Ala Gly Pro Ala Arg Thr Gly Val Gly Pro Ala Arg  
 1 5 10 15

Ile Lys Gly Ala Gln Ala Gly Trp Ala Phe His Arg Pro Ser Ala Leu  
 20 25 30

Cys Ser Arg Gly Ala Gly Gln Ala Xaa Ala Ser Glu Leu Ala Ser Arg  
 35 40 45

His Arg Gly Gly Ala Ala Ala Val Arg Thr Arg Gln Ala Asn Pro Thr  
 50 55 60

Gln Lys Ser Pro Pro Pro Asp Ser Gln Val Ala Ala Ala Ser Leu Ala  
 65 70 75 80

His Ala Glu Ser Gly Gly Ala Gly Ser Pro Leu Arg Pro Ala Ser Ala  
 85 90 95

Leu Ser Ser Ser Pro Phe Pro Phe Phe Ser Leu Ser Ser Pro Leu Ser  
 100 105 110

Leu Pro Ala Phe Ala Gln Pro Arg Ala Met Ser Asp Ala Ser Leu Arg  
 115 120 125

Ser Thr Ser Thr Met Glu Arg Leu Val Ala Arg Gly Thr Phe Pro Val  
 130 135 140

Leu Val Arg Thr Ser Ala Cys Arg Ser Leu Phe Gly Pro Val Asp His  
 145 150 155 160

Glu Glu Leu Ser Arg Glu Leu Gln Ala Arg Leu Ala Glu Leu Asn Ala  
 165 170 175

Glu Asp Gln Asn Arg Trp Asp Tyr Asp Phe Gln Gln Asp Met Pro Leu  
 180 185 190

Arg Gly Pro Gly Arg Leu Gln Trp Thr Glu Val Asp Ser Asp Ser Val  
 195 200 205

Pro Ala Phe Tyr Arg Glu Thr Val Gln Val Gly Arg Cys Arg Leu Leu  
 210 215 220

Leu Ala Pro Arg Pro Val Ala Val Ala Val Ala Val Ser Pro Pro Leu  
 225 230 235 240  
 Glu Pro Ala Ala Glu Ser Leu Asp Gly Leu Glu Glu Ala Pro Glu Gln  
 245 250 255  
 Leu Pro Ser Val Pro Val Pro Ala Pro Ala Ser Thr Pro Pro Pro Val  
 260 265 270  
 Pro Val Leu Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro Val Ala Ala  
 275 280 285  
 Pro Val Ala Ala Pro Val Ala Val Pro Val Leu Ala Pro Ala Pro Ala  
 290 295 300  
 Pro Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro Val Ala Ala Pro Ala  
 305 310 315 320  
 Pro Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro Ala Pro Ala  
 325 330 335  
 Pro Asp Ala Ala Pro Gln Glu Ser Ala Glu Gln Gly Ala Asn Gln Gly  
 340 345 350  
 Gln Arg Gly Gln Glu Pro Leu Ala Asp Gln Leu His Ser Gly Ile Ser  
 355 360 365  
 Gly Arg Pro Ala Ala Gly Thr Ala Ala Ala Ser Ala Asn Gly Ala Ala  
 370 375 380  
 Ile Lys Lys Leu Ser Gly Pro Leu Ile Ser Asp Phe Phe Ala Lys Arg  
 385 390 395 400  
 Lys Arg Ser Ala Pro Glu Lys Ser Ser Gly Asp Val Pro Ala Pro Cys  
 405 410 415  
 Pro Ser Pro Ser Ala Ala Pro Gly Val Gly Ser Val Glu Gln Thr Pro  
 420 425 430  
 Arg Lys Arg Leu Arg  
 435

<210> 153  
 <211> 172  
 <212> PRT  
 <213> Homo sapiens

<400> 153  
 Met Glu Pro Ala Ala Gly Ser Ser Met Glu Pro Ser Ala Asp Trp Leu  
 1 5 10 15  
 Ala Ser Ala Ala Ala Arg Gly Leu Val Glu Lys Val Arg Gln Leu Leu  
 20 25 30  
 Glu Ala Gly Ala Asp Pro Asn Ala Pro Asn Ser Tyr Gly Arg Arg Pro  
 35 40 45  
 Ile Gln Val Met Met Met Gly Ser Ala Arg Val Ala Glu Leu Leu Leu  
 50 55 60

Leu His Gly Ala Glu Pro Asn Cys Ala Asp Pro Ala Thr Leu Thr Arg  
 65 70 75 80  
 Pro Val His Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu Val Val  
 85 90 95  
 Leu His Arg Ala Gly Ala Arg Leu Asp Val Arg Asp Ala Trp Gly Arg  
 100 105 110  
 Leu Pro Val Asp Leu Ala Glu Glu Leu Gly His Arg Asp Val Ala Arg  
 115 120 125  
 Tyr Leu Arg Ala Ala Ala Gly Gly Thr Arg Gly Ser Asn His Ala Arg  
 130 135 140  
 Ile Asp Ala Ala Glu Gly Pro Ser Val Thr Ala Ser Ile Gln Val Pro  
 145 150 155 160  
 Gly Gly Glu Glu Gly Asp Phe Gly Ser Ser Tyr Ser  
 165 170

<210> 154  
 <211> 174  
 <212> PRT  
 <213> Homo sapiens

<400> 154  
 Met Arg Glu Glu Asn Lys Gly Met Pro Ser Gly Gly Gly Ser Asp Glu  
 1 5 10 15  
 Gly Leu Ala Ser Ala Ala Ala Arg Gly Leu Val Glu Lys Val Arg Gln  
 20 25 30  
 Leu Leu Glu Ala Gly Ala Asp Pro Asn Gly Val Asn Arg Phe Gly Arg  
 35 40 45  
 Arg Ala Ile Gln Val Met Met Met Gly Ser Ala Arg Val Ala Glu Leu  
 50 55 60  
 Leu Leu Leu His Gly Ala Glu Pro Asn Cys Ala Asp Pro Ala Thr Leu  
 65 70 75 80  
 Thr Arg Pro Val His Asp Ala Ala Arg Glu Gly Phe Leu Asp Thr Leu  
 85 90 95  
 Val Val Leu His Arg Ala Gly Ala Arg Leu Asp Val Arg Asp Ala Trp  
 100 105 110  
 Gly Arg Leu Pro Val Asp Leu Ala Glu Glu Leu Gly His Arg Asp Val  
 115 120 125  
 Ala Arg Tyr Leu Arg Ala Ala Ala Gly Gly Thr Arg Gly Ser Asn His  
 130 135 140  
 Ala Arg Ile Asp Ala Ala Glu Gly Pro Ser Val Thr Ala Ser Ile Gln  
 145 150 155 160  
 Val Pro Gly Gly Glu Glu Gly Asp Phe Gly Ser Ser Tyr Ser  
 165 170

<210> 155  
 <211> 349  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 155  
 Met Lys His Ser Leu Asn Ala Leu Leu Ile Phe Leu Ile Ile Thr Ser  
   1                  5                  10                  15  
 Ala Trp Gly Gly Ser Lys Gly Pro Leu Asp Gln Leu Glu Lys Gly Gly  
           20                  25                  30  
 Glu Thr Ala Gln Ser Ala Asp Pro Gln Trp Glu Gln Leu Asn Asn Lys  
       35                  40                  45  
 Asn Leu Ser Met Pro Leu Leu Pro Ala Asp Phe His Lys Glu Asn Thr  
   50                  55                  60  
 Val Thr Asn Asp Trp Ile Pro Glu Gly Glu Glu Asp Asp Asp Tyr Leu  
   65                  70                  75                  80  
 Asp Leu Glu Lys Ile Phe Ser Glu Asp Asp Asp Tyr Ile Asp Ile Val  
           85                  90                  95  
 Asp Ser Leu Ser Val Ser Pro Thr Asp Ser Asp Val Ser Ala Gly Asn  
       100                  105                  110  
 Ile Leu Gln Leu Phe His Gly Lys Ser Arg Ile Gln Arg Leu Asn Ile  
       115                  120                  125  
 Leu Asn Ala Lys Phe Ala Phe Asn Leu Tyr Arg Val Leu Lys Asp Gln  
       130                  135                  140  
 Val Asn Thr Phe Asp Asn Ile Phe Ile Ala Pro Val Gly Ile Ser Thr  
   145                  150                  155                  160  
 Ala Met Gly Met Ile Ser Leu Gly Leu Lys Gly Glu Thr His Glu Gln  
           165                  170                  175  
 Val His Ser Ile Leu His Phe Lys Asp Phe Val Asn Ala Ser Ser Lys  
       180                  185                  190  
 Tyr Glu Ile Thr Thr Ile His Asn Leu Phe Arg Lys Leu Thr His Arg  
       195                  200                  205  
 Leu Phe Arg Arg Asn Phe Gly Tyr Thr Leu Arg Ser Val Asn Asp Leu  
       210                  215                  220  
 Tyr Ile Gln Lys Gln Phe Pro Ile Leu Leu Asp Phe Lys Thr Lys Val  
   225                  230                  235                  240  
 Arg Glu Tyr Tyr Phe Ala Glu Ala Gln Ile Ala Asp Phe Ser Asp Pro  
           245                  250                  255  
 Ala Phe Ile Ser Lys Thr Asn Asn His Ile Met Lys Leu Thr Lys Gly  
       260                  265                  270  
 Leu Ile Lys Asp Ala Leu Glu Asn Ile Asp Pro Ala Thr Gln Met Met  
       275                  280                  285

Ile Leu Asn Cys Ile Tyr Phe Lys Gly Ser Trp Val Asn Lys Phe Pro  
 290 295 300

Val Glu Met Thr His Asn His Asn Phe Arg Leu Asn Glu Arg Glu Val  
 305 310 315 320

Val Lys Val Ser Met Met Gln Thr Lys Gly Asn Phe Leu Ala Ser Cys  
 325 330 335

Leu Leu Phe Met Gly Arg Val Ala Asn Pro Ser Arg Ser  
 340 345

<210> 156

<211> 211

<212> PRT

<213> Homo sapiens

<400> 156

Met Asp Pro Ala Arg Pro Leu Gly Leu Ser Ile Leu Leu Leu Phe Leu  
 1 5 10 15

Thr Glu Ala Ala Leu Gly Asp Ala Ala Gln Glu Pro Thr Gly Asn Asn  
 20 25 30

Ala Glu Ile Cys Leu Leu Pro Leu Asp Tyr Gly Pro Cys Arg Ala Leu  
 35 40 45

Leu Leu Arg Tyr Tyr Tyr Asp Arg Tyr Thr Gln Ser Cys Arg Gln Phe  
 50 55 60

Leu Tyr Gly Gly Cys Glu Gly Asn Ala Asn Asn Phe Tyr Thr Trp Glu  
 65 70 75 80

Ala Cys Asp Asp Ala Cys Trp Arg Ile Glu Lys Val Pro Lys Val Cys  
 85 90 95

Arg Leu Gln Val Ser Val Asp Asp Gln Cys Glu Gly Ser Thr Glu Lys  
 100 105 110

Tyr Phe Phe Asn Leu Ser Ser Met Thr Cys Glu Lys Phe Phe Ser Gly  
 115 120 125

Gly Cys His Arg Asn Arg Ile Glu Asn Arg Phe Pro Asp Glu Ala Thr  
 130 135 140

Cys Met Gly Phe Cys Ala Pro Lys Lys Ile Pro Ser Phe Cys Tyr Ser  
 145 150 155 160

Pro Lys Asp Glu Gly Leu Cys Ser Ala Asn Val Thr Arg Tyr Tyr Phe  
 165 170 175

Asn Pro Arg Tyr Arg Thr Cys Asp Ala Phe Thr Tyr Thr Gly Cys Gly  
 180 185 190

Gly Asn Asp Asn Asn Phe Val Thr Val Gln Lys Met Arg Asp Cys Ala  
 195 200 205

Leu Pro Met  
 210

<210> 157  
 <211> 210  
 <212> PRT  
 <213> Homo sapiens

<400> 157

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Met Asp Pro Ala Arg Pro Leu Gly Leu Ser Ile Leu Leu Leu Phe Leu
 1           5           10           15

Thr Glu Ala Ala Leu Gly Asp Ala Ala Gln Glu Pro Thr Gly Asn Asn
          20           25           30

Ala Glu Ile Cys Leu Leu Pro Leu Asp Tyr Gly Pro Cys Arg Ala Leu
          35           40           45

Leu Leu Arg Tyr Tyr Tyr Asp Arg Tyr Thr Gln Ser Cys Arg Gln Phe
          50           55           60

Leu Tyr Gly Gly Cys Glu Gly Asn Ala Asn Asn Phe Tyr Thr Trp Glu
          65           70           75           80

Ala Cys Asp Asp Ala Cys Trp Arg Ile Glu Lys Val Pro Lys Val Cys
          85           90           95

Arg Leu Gln Val Ser Val Asp Asp Gln Cys Glu Gly Ser Thr Glu Lys
          100          105          110

Tyr Phe Phe Asn Leu Ser Ser Met Thr Cys Glu Lys Phe Phe Ser Gly
          115          120          125

Gly Cys His Arg Asn Arg Ile Glu Asn Arg Phe Pro Asp Glu Ala Thr
          130          135          140

Cys Met Gly Phe Cys Ala Pro Lys Lys Lys Tyr Arg Thr Cys Asp Ala
          145          150          155          160

Phe Thr Tyr Thr Gly Cys Gly Gly Asn Asp Asn Asn Phe Val Ser Arg
          165          170          175

Glu Asp Cys Lys Arg Ala Cys Ala Lys Ala Leu Lys Lys Lys Lys Lys
          180          185          190

Met Pro Lys Leu Arg Phe Ala Ser Arg Ile Arg Lys Ile Arg Lys Lys
          195          200          205

Gln Phe
          210

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<210> 158  
 <211> 225  
 <212> PRT  
 <213> Homo sapiens

<400> 158

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Met Ile Tyr Thr Met Lys Lys Val His Ala Leu Trp Ala Ser Val Cys
 1           5           10           15

Leu Leu Leu Asn Leu Ala Pro Ala Pro Leu Asn Ala Asp Ser Glu Glu
          20           25           30

```

Asp Glu Glu His Thr Ile Ile Thr Asp Thr Glu Leu Pro Pro Leu Lys  
                   35                                  40                                  45  
 Leu Met His Ser Phe Cys Ala Phe Lys Ala Asp Asp Gly Pro Cys Lys  
                   50                                  55                                  60  
 Ala Ile Met Lys Arg Phe Phe Phe Asn Ile Phe Thr Arg Gln Cys Glu  
                   65                                  70                                  75                                  80  
 Glu Phe Ile Tyr Gly Gly Cys Glu Gly Asn Gln Asn Arg Phe Glu Ser  
                                   85                                  90                                  95  
 Leu Glu Glu Cys Lys Lys Met Cys Thr Arg Asp Asn Ala Asn Arg Ile  
                                   100                                  105                                  110  
 Ile Lys Thr Thr Leu Gln Gln Glu Lys Pro Asp Phe Cys Phe Leu Glu  
                                   115                                  120                                  125  
 Glu Asp Pro Gly Ile Cys Arg Gly Tyr Ile Thr Arg Tyr Phe Tyr Asn  
                   130                                  135                                  140  
 Asn Gln Thr Lys Gln Cys Glu Arg Phe Lys Tyr Gly Gly Cys Leu Gly  
                   145                                  150                                  155                                  160  
 Asn Met Asn Asn Phe Glu Thr Leu Glu Glu Cys Lys Asn Ile Cys Glu  
                                   165                                  170                                  175  
 Asp Gly Pro Asn Gly Phe Gln Val Asp Asn Tyr Gly Thr Gln Leu Asn  
                                   180                                  185                                  190  
 Ala Val Asn Asn Ser Leu Thr Pro Gln Ser Thr Lys Val Pro Ser Leu  
                   195                                  200                                  205  
 Phe Gly Lys Asn Leu Val Asp Phe Ile Ala Ser Arg Lys Leu Leu Ser  
                   210                                  215                                  220  
 Cys  
 225

<210> 159  
 <211> 636  
 <212> PRT  
 <213> Homo sapiens

<400> 159  
 Met Ala Ser Arg Leu Thr Leu Leu Thr Leu Leu Leu Leu Leu Ala  
           1                                  5                                  10                                  15  
 Gly Asp Arg Ala Ser Ser Asn Pro Asn Ala Thr Ser Ser Ser Ser Gln  
                   20                                  25                                  30  
 Asp Pro Glu Ser Leu Gln Asp Arg Gly Glu Gly Lys Val Ala Thr Thr  
                   35                                  40                                  45  
 Val Ile Ser Lys Met Leu Phe Val Glu Pro Ile Leu Glu Val Ser Ser  
                   50                                  55                                  60  
 Leu Pro Thr Thr Asn Ser Thr Thr Asn Ser Ala Thr Lys Ile Thr Ala  
                   65                                  70                                  75                                  80



Asn Thr Thr Asp Glu Pro Thr Thr Gln Pro Thr Thr Glu Pro Thr Thr  
 85 90 95  
 Gln Pro Thr Ile Gln Pro Thr Gln Pro Thr Thr Gln Leu Pro Thr Asp  
 100 105 110  
 Ser Pro Thr Gln Pro Thr Thr Gly Ser Phe Cys Pro Gly Pro Val Thr  
 115 120 125  
 Leu Cys Ser Asp Leu Glu Ser His Ser Thr Glu Ala Val Leu Gly Asp  
 130 135 140  
 Ala Leu Val Asp Phe Ser Leu Lys Leu Tyr His Ala Phe Ser Ala Met  
 145 150 155 160  
 Lys Lys Val Glu Thr Asn Met Ala Phe Ser Pro Phe Ser Ile Ala Ser  
 165 170 175  
 Leu Leu Thr Gln Val Leu Leu Gly Ala Gly Glu Asn Thr Lys Thr Asn  
 180 185 190  
 Leu Glu Ser Ile Leu Ser Tyr Pro Lys Asp Phe Thr Cys Val His Gln  
 195 200 205  
 Ala Leu Lys Gly Phe Thr Thr Lys Gly Val Thr Ser Val Ser Gln Ile  
 210 215 220  
 Phe His Ser Pro Val Asp Trp Arg Leu Leu Gln Ser Lys Ser Gln Glu  
 225 230 235 240  
 Val Leu Ser Gln Thr Ser Thr Lys Ala Arg Lys Gln Ser Leu Phe Arg  
 245 250 255  
 Ala Lys Ile Lys Gly Arg Lys Glu Gly Lys Ser Arg Gln Met Glu Phe  
 260 265 270  
 Asn Ile Ser Lys Arg Leu Ser Cys Arg Ala Ile Val His Ser Lys Leu  
 275 280 285  
 Arg Gln Arg Arg Leu Gly Ala Thr Ser Leu Val Leu Gly Ser Gly Phe  
 290 295 300  
 Thr Phe Phe Gly Pro Tyr Leu Pro His Leu Glu Glu Glu Trp Ala Gly  
 305 310 315 320  
 Pro Arg Ser Thr Met Pro Tyr Ser Leu Ser Glu Gln Ile Glu Pro Lys  
 325 330 335  
 Lys Ala Cys Ser Leu Ser Asn Cys Ala His Gly Lys Asn Asp Val Phe  
 340 345 350  
 Arg Thr Tyr Cys Phe Pro Phe Leu Lys Tyr Pro Pro Asp Leu Ala Ile  
 355 360 365  
 Arg Asp Thr Phe Val Asn Ala Ser Arg Thr Leu Tyr Ser Ser Ser Pro  
 370 375 380  
 Arg Val Leu Ser Asn Asn Ser Asp Ala Asn Leu Glu Leu Ile Asn Thr  
 385 390 395 400

Trp Val Ala Lys Asn Thr Asn Asn Lys Ile Ser Arg Leu Leu Asp Ser  
 405 410 415  
 Leu Pro Ser Asp Thr Arg Leu Val Leu Leu Asn Ala Ile Tyr Leu Ser  
 420 425 430  
 Ala Lys Trp Lys Thr Thr Phe Asp Pro Lys Lys Thr Arg Met Glu Pro  
 435 440 445  
 Phe His Phe Lys Asn Ser Val Ile Lys Val Pro Met Met Asn Ser Lys  
 450 455 460  
 Lys Tyr Pro Val Ala His Phe Ile Asp Gln Thr Leu Lys Ala Lys Val  
 465 470 475 480  
 Gly Gln Leu Gln Leu Ser His Asn Leu Ser Leu Val Ile Leu Val Pro  
 485 490 495  
 Gln Asn Leu Lys His Arg Leu Glu Asp Met Glu Gln Ala Leu Ser Pro  
 500 505 510  
 Ser Val Phe Lys Ala Ile Met Glu Lys Leu Glu Met Ser Lys Phe Gln  
 515 520 525  
 Pro Thr Leu Leu Thr Leu Pro Arg Ile Lys Val Thr Thr Ser Gln Asp  
 530 535 540  
 Met Leu Ser Ile Met Glu Lys Leu Glu Phe Phe Asp Phe Ser Tyr Asp  
 545 550 555 560  
 Leu Asn Leu Cys Gly Leu Thr Glu Asp Pro Asp Leu Gln Val Ser Ala  
 565 570 575  
 Met Gln His Gln Thr Val Leu Glu Leu Thr Glu Thr Gly Val Glu Ala  
 580 585 590  
 Ala Ala Ala Ser Ala Ile Ser Val Ala Arg Thr Leu Leu Val Phe Glu  
 595 600 605  
 Val Gln Gln Pro Phe Leu Phe Val Leu Trp Asp Gln Gln His Lys Phe  
 610 615 620  
 Pro Val Phe Met Gly Arg Val Tyr Asp Pro Arg Ala  
 625 630 635

&lt;210&gt; 160

&lt;211&gt; 389

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 160

Met Asp Val Leu Ala Glu Ala Asn Gly Thr Phe Ala Leu Asn Leu Leu  
 1 5 10 15

Lys Thr Leu Gly Lys Asp Asn Ser Lys Asn Val Phe Phe Ser Pro Met  
 20 25 30

Ser Met Ser Cys Ala Leu Ala Met Val Tyr Met Gly Ala Lys Gly Asn  
 35 40 45

Thr Ala Ala Gln Met Ala Gln Ile Leu Ser Phe Asn Lys Ser Gly Gly  
 50 55 60  
 Gly Gly Asp Ile His Gln Gly Phe Gln Ser Leu Leu Thr Glu Val Asn  
 65 70 75 80  
 Lys Thr Gly Thr Gln Tyr Leu Leu Arg Met Ala Asn Arg Leu Phe Gly  
 85 90 95  
 Glu Lys Ser Cys Asp Phe Leu Ser Ser Phe Arg Asp Ser Cys Gln Lys  
 100 105 110  
 Phe Tyr Gln Ala Glu Met Glu Glu Leu Asp Phe Ile Ser Ala Val Glu  
 115 120 125  
 Lys Ser Arg Lys His Ile Asn Thr Trp Val Ala Glu Lys Thr Glu Gly  
 130 135 140  
 Lys Ile Ala Glu Leu Leu Ser Pro Gly Ser Val Asp Pro Leu Thr Arg  
 145 150 155 160  
 Leu Val Leu Val Asn Ala Val Tyr Phe Arg Gly Asn Trp Asp Glu Gln  
 165 170 175  
 Phe Asp Lys Glu Asn Thr Glu Glu Arg Leu Phe Lys Val Ser Lys Asn  
 180 185 190  
 Glu Glu Lys Pro Val Gln Met Met Phe Lys Gln Ser Thr Phe Lys Lys  
 195 200 205  
 Thr Tyr Ile Gly Glu Ile Phe Thr Gln Ile Leu Val Leu Pro Tyr Val  
 210 215 220  
 Gly Lys Glu Leu Asn Met Ile Ile Met Leu Pro Asp Glu Thr Thr Asp  
 225 230 235 240  
 Leu Arg Thr Val Glu Lys Glu Leu Thr Tyr Glu Lys Phe Val Glu Trp  
 245 250 255  
 Thr Arg Leu Asp Met Met Asp Glu Glu Glu Val Glu Val Ser Leu Pro  
 260 265 270  
 Arg Phe Lys Leu Glu Glu Ser Tyr Asp Met Glu Ser Val Leu Arg Asn  
 275 280 285  
 Leu Gly Met Thr Asp Ala Phe Glu Leu Gly Lys Ala Asp Phe Ser Gly  
 290 295 300  
 Met Ser Gln Thr Asp Leu Ser Leu Ser Lys Val Val His Lys Ser Phe  
 305 310 315 320  
 Val Glu Val Asn Glu Glu Gly Thr Glu Ala Ala Ala Ala Thr Ala Ala  
 325 330 335  
 Ile Met Met Met Arg Cys Ala Arg Phe Val Pro Arg Phe Cys Ala Asp  
 340 345 350  
 His Pro Phe Leu Phe Phe Ile Gln His Ser Cys Pro Leu Thr Leu His  
 355 360 365  
 Ser Val Pro Ala Thr Gln Val Ala Leu Ser Val Gln Trp Trp Gln Phe

370

375

380

Arg Asn Lys Gly Pro  
385

<210> 161  
<211> 204  
<212> PRT  
<213> Homo sapiens

&lt;400&gt; 161

Met Asp Val Leu Ala Glu Ala Asn Gly Thr Phe Ala Leu Asn Leu Leu  
1 5 10 15

Lys Thr Leu Gly Lys Asp Asn Ser Lys Asn Val Phe Phe Ser Pro Met  
20 25 30

Ser Met Ser Cys Ala Leu Ala Met Val Tyr Met Gly Ala Lys Gly Asn  
35 40 45

Thr Ala Ala Gln Met Ala Gln Ile Leu Ser Phe Asn Lys Ser Gly Gly  
50 55 60

Gly Gly Asp Ile His Gln Gly Phe Gln Ser Leu Leu Thr Glu Val Asn  
65 70 75 80

Lys Thr Gly Thr Gln Tyr Leu Leu Arg Met Ala Asn Arg Leu Phe Gly  
85 90 95

Glu Lys Ser Cys Asp Phe Leu Ser Ser Phe Arg Asp Ser Cys Gln Lys  
100 105 110

Phe Tyr Gln Ala Glu Met Glu Glu Leu Asp Phe Ile Ser Ala Val Glu  
115 120 125

Lys Ser Arg Lys His Ile Asn Thr Trp Val Ala Glu Lys Thr Glu Gly  
130 135 140

Lys Ile Ala Glu Leu Leu Ser Pro Gly Ser Val Asp Pro Leu Thr Arg  
145 150 155 160

Leu Val Leu Val Asn Ala Val Tyr Phe Arg Gly Asn Trp Asp Glu Gln  
165 170 175

Phe Asp Lys Glu Asn Thr Glu Glu Arg Leu Phe Lys Val Ser Lys Thr  
180 185 190

Asn Gly Ile Leu Phe Cys Gly Arg Phe Ser Ser Pro  
195 200

<210> 162  
<211> 156  
<212> PRT  
<213> Homo sapiens

&lt;400&gt; 162

Met Asp Val Leu Ala Glu Ala Asn Gly Thr Phe Ala Leu Asn Leu Leu  
1 5 10 15

Lys Thr Leu Gly Lys Asp Asn Ser Lys Asn Val Phe Phe Ser Pro Met  
                   20                                  25                                  30  
 Ser Met Ser Cys Ala Leu Ala Met Val Tyr Met Gly Ala Lys Gly Asn  
                   35                                  40                                  45  
 Thr Ala Ala Gln Met Ala Gln Ile Leu Ser Phe Asn Lys Ser Gly Gly  
                   50                                  55                                  60  
 Gly Gly Asp Ile His Gln Gly Phe Gln Ser Leu Leu Thr Glu Val Asn  
                   65                                  70                                  75                                  80  
 Lys Thr Gly Thr Gln Tyr Leu Leu Arg Met Ala Asn Arg Leu Phe Gly  
                                   85                                  90                                  95  
 Glu Lys Ser Cys Asp Phe Leu Ser Ser Phe Arg Asp Ser Cys Gln Lys  
                                   100                                  105                                  110  
 Phe Tyr Gln Ala Glu Met Glu Glu Leu Asp Phe Ile Ser Ala Val Glu  
                   115                                  120                                  125  
 Lys Ser Arg Lys His Ile Asn Thr Trp Val Ala Glu Lys Thr Glu Gly  
                   130                                  135                                  140  
 Lys Met Tyr Cys Tyr Ser Thr Phe Val Ile Thr Ser  
                   145                                  150                                  155

<210> 163  
 <211> 517  
 <212> PRT  
 <213> Homo sapiens

<400> 163  
 Met Ala Ala Leu Met Thr Pro Gly Thr Gly Ala Pro Pro Ala Pro Gly  
   1                                  5                                  10                                  15  
 Asp Phe Ser Gly Glu Gly Ser Gln Gly Leu Pro Asp Pro Ser Pro Glu  
                   20                                  25                                  30  
 Pro Lys Gln Leu Pro Glu Leu Ile Arg Met Lys Arg Asp Gly Gly Arg  
                   35                                  40                                  45  
 Leu Ser Glu Ala Asp Ile Arg Gly Phe Val Ala Ala Val Val Asn Gly  
                   50                                  55                                  60  
 Ser Ala Gln Gly Ala Gln Ile Gly Ala Met Leu Met Ala Ile Arg Leu  
                   65                                  70                                  75                                  80  
 Arg Gly Met Asp Leu Glu Glu Thr Ser Val Leu Thr Gln Ala Leu Ala  
                                   85                                  90                                  95  
 Gln Ser Gly Gln Gln Leu Glu Trp Pro Glu Ala Trp Arg Gln Gln Leu  
                   100                                  105                                  110  
 Val Asp Lys His Ser Thr Gly Gly Val Gly Asp Lys Val Ser Leu Val  
                   115                                  120                                  125  
 Leu Ala Pro Ala Leu Ala Ala Cys Gly Cys Lys Val Pro Met Ile Ser  
                   130                                  135                                  140

Gly Arg Gly Leu Gly His Thr Gly Gly Thr Leu Asp Lys Leu Glu Ser  
 145 150 155 160  
 Ile Pro Gly Phe Asn Val Ile Gln Ser Pro Glu Gln Met Gln Val Leu  
 165 170 175  
 Leu Asp Gln Ala Gly Cys Cys Ile Val Gly Gln Ser Glu Gln Leu Val  
 180 185 190  
 Pro Ala Asp Gly Ile Leu Tyr Ala Ala Arg Asp Val Thr Ala Thr Val  
 195 200 205  
 Asp Ser Leu Pro Leu Ile Thr Ala Ser Ile Leu Ser Lys Lys Leu Val  
 210 215 220  
 Glu Gly Leu Ser Ala Leu Val Val Asp Val Lys Phe Gly Gly Ala Ala  
 225 230 235 240  
 Val Phe Pro Asn Gln Glu Gln Ala Arg Glu Leu Ala Lys Thr Leu Val  
 245 250 255  
 Gly Val Gly Ala Ser Leu Gly Leu Arg Val Ala Ala Ala Leu Thr Ala  
 260 265 270  
 Met Asp Lys Pro Leu Gly Arg Cys Val Gly His Ala Leu Glu Val Glu  
 275 280 285  
 Glu Ala Leu Leu Cys Met Asp Gly Ala Gly Pro Pro Asp Leu Arg Asp  
 290 295 300  
 Leu Val Thr Thr Leu Gly Gly Ala Leu Leu Trp Leu Ser Gly His Ala  
 305 310 315 320  
 Gly Thr Gln Ala Gln Gly Ala Ala Arg Val Ala Ala Ala Leu Asp Asp  
 325 330 335  
 Gly Ser Ala Leu Gly Arg Phe Glu Arg Met Leu Ala Ala Gln Gly Val  
 340 345 350  
 Asp Pro Gly Leu Ala Arg Ala Leu Cys Ser Gly Ser Pro Ala Glu Arg  
 355 360 365  
 Arg Gln Leu Leu Pro Arg Ala Arg Glu Gln Glu Glu Leu Leu Ala Pro  
 370 375 380  
 Ala Asp Gly Glu Arg Ser Gly Glu Ser Pro Ser Phe Arg Leu Arg His  
 385 390 395 400  
 Pro Leu Pro Phe Pro Arg Pro Arg Pro Phe Pro Ser Pro Arg Leu Ser  
 405 410 415  
 Ala Pro Leu Pro Ala Gly Thr Val Glu Leu Val Arg Ala Leu Pro Leu  
 420 425 430  
 Ala Leu Val Leu His Glu Leu Gly Ala Gly Arg Ser Arg Ala Gly Glu  
 435 440 445  
 Pro Leu Arg Leu Gly Val Gly Ala Glu Leu Leu Val Asp Val Gly Gln  
 450 455 460  
 Arg Leu Arg Arg Gly Thr Pro Trp Leu Arg Val His Arg Asp Gly Pro

[illegible]

```
<210> 164
<211> 142
<212> PRT
<213> Homo sapiens
```

```

<400> 164
Met Ser Asp Ala Ser Leu Arg Ser Thr Ser Thr Met Glu Arg Leu Val
  1              5              10              15
Ala Arg Gly Thr Phe Pro Val Leu Val Arg Thr Ser Ala Cys Arg Ser
      20              25              30
Leu Phe Gly Pro Val Asp His Glu Glu Leu Ser Arg Glu Leu Gln Ala
      35              40              45
Arg Leu Ala Glu Leu Asn Ala Glu Asp Gln Asn Arg Trp Asp Tyr Asp
      50              55              60
Phe Gln Gln Asp Met Pro Leu Arg Gly Pro Gly Arg Leu Gln Trp Thr
      65              70              75              80
Glu Val Asp Ser Asp Ser Val Pro Ala Phe Tyr Arg Glu Thr Val Gln
      85              90              95
Ile Ser Ser Pro Ser Ala Arg Asp Gln Arg Leu Arg Ser Arg Arg Ala
      100              105              110
Met Ser Pro Arg Arg Val Pro Leu Gln Ala Pro Pro Leu Ala Trp Ala
      115              120              125
Arg Trp Ser Arg Pro Arg Ala Arg Gly Cys Gly Glu Pro Ile
      130              135              140

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```
<210> 165
<211> 561
<212> PRT
<213> Homo sapiens
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<400> 165  
Met Gly Ala Pro Ala Cys Ala Leu Ala Leu Cys Val Ala Val Ala Ile  
1 5 10 15  
Val Ala Gly Ala Ser Ser Glu Ser Leu Gly Thr Glu Gln Arg Val Val  
20 25 30  
Gly Arg Ala Ala Glu Val Pro Gly Pro Glu Pro Gly Gln Gln Glu Gln  
35 40 45

Leu Val Phe Gly Ser Gly Asp Ala Val Glu Leu Ser Cys Pro Pro Pro  
 50 55 60  
 Gly Gly Gly Pro Met Gly Pro Thr Val Trp Val Lys Asp Gly Thr Gly  
 65 70 75 80  
 Leu Val Pro Ser Glu Arg Val Leu Val Gly Pro Gln Arg Leu Gln Val  
 85 90 95  
 Leu Asn Ala Ser His Glu Asp Ser Gly Ala Tyr Ser Cys Arg Gln Arg  
 100 105 110  
 Leu Thr Gln Arg Val Leu Cys His Phe Ser Val Arg Val Thr Asp Ala  
 115 120 125  
 Pro Ser Ser Gly Asp Asp Glu Asp Gly Glu Asp Glu Ala Glu Asp Thr  
 130 135 140  
 Gly Val Asp Thr Gly Ala Pro Tyr Trp Thr Arg Pro Glu Arg Met Asp  
 145 150 155 160  
 Lys Lys Leu Leu Ala Val Pro Ala Ala Asn Thr Val Arg Phe Arg Cys  
 165 170 175  
 Pro Ala Ala Gly Asn Pro Thr Pro Ser Ile Ser Trp Leu Lys Asn Gly  
 180 185 190  
 Arg Glu Phe Arg Gly Glu His Arg Ile Gly Gly Ile Lys Leu Arg His  
 195 200 205  
 Gln Gln Trp Ser Leu Val Met Glu Ser Val Val Pro Ser Asp Arg Gly  
 210 215 220  
 Asn Tyr Thr Cys Val Val Glu Asn Lys Phe Gly Ser Ile Arg Gln Thr  
 225 230 235 240  
 Tyr Thr Leu Asp Val Leu Glu Arg Ser Pro His Arg Pro Ile Leu Gln  
 245 250 255  
 Ala Gly Leu Pro Ala Asn Gln Thr Ala Val Leu Gly Ser Asp Val Glu  
 260 265 270  
 Phe His Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile Gln Trp Leu  
 275 280 285  
 Lys His Val Glu Val Asn Gly Ser Lys Val Gly Pro Asp Gly Thr Pro  
 290 295 300  
 Tyr Val Thr Val Leu Lys Thr Ala Gly Ala Asn Thr Thr Asp Lys Glu  
 305 310 315 320  
 Leu Glu Val Leu Ser Leu His Asn Val Thr Phe Glu Asp Ala Gly Glu  
 325 330 335  
 Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Phe Ser His His Ser Ala  
 340 345 350  
 Trp Leu Val Val Leu Pro Ala Glu Glu Glu Leu Val Glu Ala Asp Glu  
 355 360 365  
 Ala Gly Ser Val Tyr Ala Gly Ile Leu Ser Tyr Gly Val Gly Phe Phe



370                      375                      380  
 Leu Phe Ile Leu Val Val Ala Ala Val Thr Xaa Cys Arg Leu Arg Ser  
 385                      390                      395                      400  
 Pro Pro Lys Lys Gly Leu Gly Ser Pro Thr Val His Lys Ile Ser Arg  
                     405                      410                      415  
 Phe Pro Leu Lys Arg Gln Val Ser Leu Glu Ser Asn Ala Ser Met Ser  
                     420                      425                      430  
 Ser Asn Thr Pro Leu Val Arg Ile Ala Arg Leu Ser Ser Gly Glu Gly  
                     435                      440                      445  
 Pro Thr Leu Ala Asn Val Ser Glu Leu Glu Leu Pro Ala Asp Pro Lys  
                     450                      455                      460  
 Trp Glu Leu Ser Arg Ala Arg Leu Thr Leu Gly Lys Pro Leu Gly Glu  
 465                      470                      475                      480  
 Gly Cys Phe Gly Gln Val Val Met Ala Glu Ala Ile Gly Ile Asp Lys  
                     485                      490                      495  
 Asp Arg Ala Ala Lys Pro Val Thr Val Ala Val Lys Met Leu Lys Asp  
                     500                      505                      510  
 Asp Ala Thr Asp Lys Asp Leu Ser Asp Leu Val Ser Glu Met Glu Met  
                     515                      520                      525  
 Met Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gln Val  
                     530                      535                      540  
 Pro Met Leu Leu Asp Val Thr Ser Leu Tyr Ile Ser Ile Tyr Ile Ile  
 545                      550                      555                      560  
 Tyr

<210> 166  
 <211> 188  
 <212> PRT  
 <213> Homo sapiens

<400> 166  
 Met Asp Pro Ala Arg Pro Leu Gly Leu Ser Ile Leu Leu Leu Phe Leu  
   1                    5                    10                    15  
 Thr Glu Ala Ala Leu Gly Asp Ala Ala Gln Glu Pro Thr Gly Asn Asn  
                     20                    25                    30  
 Ala Glu Ile Cys Leu Leu Pro Leu Asp Tyr Gly Pro Cys Arg Ala Leu  
                     35                    40                    45  
 Leu Leu Arg Tyr Tyr Tyr Asp Arg Tyr Thr Gln Ser Cys Arg Gln Phe  
                     50                    55                    60  
 Leu Tyr Gly Gly Cys Glu Gly Asn Arg Asn Asn Phe Tyr Thr Trp Glu  
                     65                    70                    75                    80  
 Ala Cys Asp Asp Ala Cys Trp Arg Ile Glu Lys Val Pro Lys Val Cys

85 90 95  
 Arg Leu Gln Val Ser Val Asp Asp Gln Cys Glu Gly Ser Thr Glu Lys  
 100 105 110  
 Tyr Phe Phe Asn Leu Ser Ser Met Thr Cys Glu Lys Phe Phe Ser Gly  
 115 120 125  
 Gly Cys His Arg Asn Arg Ile Glu Asn Arg Phe Pro Asp Glu Ala Thr  
 130 135 140  
 Cys Met Gly Phe Cys Ala Pro Lys Lys Ile Pro Ser Phe Cys Tyr Ser  
 145 150 155 160  
 Pro Lys Asp Glu Gly Leu Cys Ser Ala Asn Val Thr Arg Tyr Tyr Phe  
 165 170 175  
 Asn Ile Asp Val Ser Ile Ser Thr Ala Val Lys Leu  
 180 185  
  
 <210> 167  
 <211> 539  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 167  
 Met Asn Gln Leu Arg Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg  
 1 5 10 15  
 Ser Ala Gly Trp Asn Ile Pro Ile Gly Leu Leu Tyr Cys Asp Leu Pro  
 20 25 30  
 Glu Pro Arg Lys Pro Leu Glu Lys Ala Val Ala Asn Phe Phe Ser Gly  
 35 40 45  
 Ser Cys Ala Pro Cys Ala Asp Gly Thr Asp Phe Pro Gln Leu Cys Gln  
 50 55 60  
 Leu Cys Pro Gly Cys Gly Cys Ser Thr Leu Asn Gln Tyr Phe Gly Tyr  
 65 70 75 80  
 Ser Gly Ala Phe Lys Cys Leu Lys Asp Gly Ala Gly Asp Val Ala Phe  
 85 90 95  
 Val Lys His Ser Thr Ile Phe Glu Asn Leu Ala Asn Lys Ala Asp Arg  
 100 105 110  
 Asp Gln Tyr Glu Leu Leu Cys Leu Asp Asn Thr Arg Lys Pro Val Asp  
 115 120 125  
 Glu Tyr Lys Asp Cys His Leu Ala Gln Val Pro Ser His Thr Val Val  
 130 135 140  
 Ala Arg Ser Met Gly Gly Lys Glu Asp Leu Ile Trp Glu Leu Leu Asn  
 145 150 155 160  
 Gln Ala Gln Glu His Phe Gly Lys Asp Lys Ser Lys Glu Phe Gln Leu  
 165 170 175  
 Phe Ser Ser Pro His Gly Lys Asp Leu Leu Phe Lys Asp Ser Ala His

180					185					190					
Gly	Phe	Leu	Lys	Val	Pro	Pro	Arg	Met	Asp	Ala	Lys	Met	Tyr	Leu	Gly
		195					200					205			
Tyr	Glu	Tyr	Val	Thr	Ala	Ile	Arg	Asn	Leu	Arg	Glu	Gly	Thr	Cys	Pro
	210					215					220				
Glu	Ala	Pro	Thr	Asp	Glu	Cys	Lys	Pro	Val	Lys	Trp	Cys	Ala	Leu	Ser
225					230					235					240
His	His	Glu	Arg	Leu	Lys	Cys	Asp	Glu	Trp	Ser	Val	Asn	Ser	Val	Gly
				245					250					255	
Lys	Ile	Glu	Cys	Val	Ser	Ala	Glu	Thr	Thr	Glu	Asp	Cys	Ile	Ala	Lys
			260					265					270		
Ile	Met	Asn	Gly	Glu	Ala	Asp	Ala	Met	Ser	Leu	Asp	Gly	Gly	Phe	Val
		275					280					285			
Tyr	Ile	Ala	Gly	Lys	Cys	Gly	Leu	Val	Pro	Val	Leu	Ala	Glu	Asn	Tyr
	290					295					300				
Asn	Lys	Ser	Asp	Asn	Cys	Glu	Asp	Thr	Pro	Glu	Ala	Gly	Tyr	Phe	Ala
305					310					315					320
Val	Ala	Val	Val	Lys	Lys	Ser	Ala	Ser	Asp	Leu	Thr	Trp	Asp	Asn	Leu
				325					330					335	
Lys	Gly	Lys	Lys	Ser	Cys	His	Thr	Ala	Val	Gly	Arg	Thr	Ala	Gly	Trp
			340					345					350		
Asn	Ile	Pro	Met	Gly	Leu	Leu	Tyr	Asn	Lys	Ile	Asn	His	Cys	Glu	Pro
		355					360					365			
Asn	Asn	Lys	Glu	Gly	Tyr	Tyr	Gly	Tyr	Thr	Gly	Ala	Phe	Arg	Cys	Leu
	370					375					380				
Val	Glu	Lys	Gly	Asp	Val	Ala	Phe	Val	Lys	His	Gln	Thr	Val	Pro	Gln
385					390					395					400
Asn	Thr	Gly	Gly	Lys	Asn	Pro	Asp	Pro	Trp	Ala	Lys	Asn	Leu	Asn	Glu
				405					410					415	
Lys	Asp	Tyr	Glu	Leu	Leu	Cys	Leu	Asp	Gly	Thr	Arg	Lys	Pro	Val	Glu
			420					425					430		
Glu	Tyr	Ala	Asn	Cys	His	Leu	Ala	Arg	Ala	Pro	Asn	His	Ala	Val	Val
		435					440					445			
Thr	Arg	Lys	Asp	Lys	Glu	Ala	Cys	Val	His	Lys	Ile	Leu	Arg	Gln	Gln
	450					455					460				
Gln	His	Leu	Phe	Gly	Ser	Asn	Val	Thr	Asp	Cys	Ser	Gly	Asn	Phe	Cys
465					470					475					480
Leu	Phe	Arg	Ser	Glu	Thr	Lys	Asp	Leu	Leu	Phe	Arg	Asp	Asp	Thr	Val
				485					490					495	
Cys	Leu	Ala	Lys	Leu	His	Asp	Arg	Asn	Thr	Tyr	Glu	Lys	Tyr	Leu	Gly
			500					505					510		

Glu Glu Tyr Val Lys Ala Val Gly Asn Leu Arg Lys Cys Ser Thr Ser  
 515 520 525

Ser Leu Leu Glu Ala Cys Thr Phe Arg Arg Pro  
 530 535

<210> 168

<211> 77

<212> PRT

<213> Homo sapiens

<400> 168

Met Arg Thr Leu Leu Pro Pro Ala Leu Leu Thr Cys Trp Leu Leu Ala  
 1 5 10 15

Pro Val Asn Ser Ile His Pro Glu Cys Arg Phe His Leu Glu Ile Gln  
 20 25 30

Glu Glu Glu Thr Lys Cys Ala Glu Leu Leu Arg Ser Gln Thr Glu Lys  
 35 40 45

His Lys Gly His Thr Lys Gly Phe Ile Leu Ile His Ala Gly Gly Leu  
 50 55 60

Lys Arg Ile Leu Asp Pro His Thr Tyr Pro Leu Ala Pro  
 65 70 75

<210> 169

<211> 161

<212> PRT

<213> Homo sapiens

<400> 169

Met Lys Leu Pro Glu Val Cys Phe Phe Asn Cys Cys Thr Leu His Glu  
 1 5 10 15

Ser Lys Tyr Glu Ile Val Thr Met Phe Ile Tyr Phe Asn Trp Leu Tyr  
 20 25 30

Phe Phe Pro Ala Asn Gly Phe Gln Val Asp Asn Tyr Gly Thr Gln Leu  
 35 40 45

Asn Ala Val Asn Asn Ser Leu Thr Pro Gln Ser Thr Lys Val Pro Ser  
 50 55 60

Leu Phe Glu Phe His Gly Pro Ser Trp Cys Leu Thr Pro Ala Asp Arg  
 65 70 75 80

Gly Leu Cys Arg Ala Asn Glu Asn Arg Phe Tyr Tyr Asn Ser Val Ile  
 85 90 95

Gly Lys Cys Arg Pro Phe Lys Tyr Ser Gly Cys Gly Gly Asn Glu Asn  
 100 105 110

Asn Phe Thr Ser Lys Gln Glu Cys Leu Arg Ala Cys Lys Lys Gly Phe  
 115 120 125

Ile Gln Arg Ile Ser Lys Gly Gly Leu Ile Lys Thr Lys Arg Lys Arg

130

135

140

Lys Lys Gln Arg Val Lys Ile Ala Tyr Glu Glu Ile Phe Val Lys Asn  
 145 150 155 160

Met

&lt;210&gt; 170

&lt;211&gt; 157

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 170

Met Tyr Asn Thr Ser Xaa Met Xaa Pro Xaa Asn Pro Arg Pro Ile Leu  
 1 5 10 15

Thr Ile Ile Thr Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asp  
 20 25 30

Ser Phe Glu Val Arg Val Cys Ala Ser Pro Gly Arg Asp Pro Arg Thr  
 35 40 45

Glu Glu Glu Asn Phe Arg Lys Lys Glu Val Leu Cys Pro Glu Leu Pro  
 50 55 60

Pro Gly Ser Ala Lys Arg Ala Leu Pro Thr Cys Thr Ser Ala Ser Pro  
 65 70 75 80

Pro Gln Lys Lys Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Lys Ile  
 85 90 95

Arg Gly Arg Lys Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu  
 100 105 110

Glu Leu Lys Asp Ala His Ala Thr Glu Glu Ser Gly Asp Ser Arg Ala  
 115 120 125

His Ser Ser Tyr Leu Lys Thr Lys Lys Gly Gln Ser Thr Ser Arg His  
 130 135 140

Lys Lys Thr Met Val Lys Lys Val Gly Pro Asp Ser Asp  
 145 150 155

&lt;210&gt; 171

&lt;211&gt; 157

&lt;212&gt; PRT

&lt;213&gt; Mouse

&lt;400&gt; 171

Met Phe Asn Arg Ser Cys Leu Arg Gly Met Asn Pro Arg Pro Ile Leu  
 1 5 10 15

Thr Ile Ile Thr Leu Glu Asp Ser Ser Gly Asn Leu Leu Gly Arg Asp  
 20 25 30

Ser Phe Glu Val Arg Val Cys Ala Ser Pro Gly Arg Asp Pro Arg Thr  
 35 40 45

Glu Glu Glu Asn Phe Arg Lys Lys Glu Val Leu Cys Pro Glu Leu Pro  
 50 55 60  
 Pro Gly Ser Ala Lys Arg Ala Leu Pro Thr Cys Thr Ser Ala Ser Pro  
 65 70 75 80  
 Pro Gln Lys Lys Lys Pro Leu Asp Gly Glu Tyr Phe Thr Leu Lys Ile  
 85 90 95  
 Arg Gly Arg Lys Arg Phe Glu Met Phe Arg Glu Leu Asn Glu Ala Leu  
 100 105 110  
 Glu Leu Lys Asp Ala His Ala Thr Glu Glu Ser Gly Asp Ser Arg Ala  
 115 120 125  
 His Ser Ser Tyr Leu Lys Thr Lys Lys Gly Gln Ser Thr Ser Arg His  
 130 135 140  
 Lys Lys Thr Met Val Lys Lys Val Gly Pro Asp Ser Asp  
 145 150 155

<210> 172  
 <211> 1252  
 <212> PRT  
 <213> Mouse

<400> 172

Met Gly Ala Ala Ser Gly Gln Arg Gly Arg Trp Pro Leu Ser Pro Pro  
 1 5 10 15  
 Leu Leu Met Leu Ser Leu Leu Val Leu Leu Leu Gln Pro Ser Pro Ala  
 20 25 30  
 Pro Ala Leu Asp Pro Gly Leu Gln Pro Gly Asn Phe Ser Pro Asp Glu  
 35 40 45  
 Ala Gly Ala Gln Leu Phe Ala Glu Ser Tyr Asn Ser Ser Ala Glu Val  
 50 55 60  
 Val Met Phe Gln Ser Thr Val Ala Ser Trp Ala His Asp Thr Asn Ile  
 65 70 75 80  
 Thr Glu Glu Asn Ala Arg Arg Gln Glu Glu Ala Ala Leu Val Ser Gln  
 85 90 95  
 Glu Phe Ala Glu Val Trp Gly Lys Lys Ala Lys Glu Leu Tyr Glu Ser  
 100 105 110  
 Ile Trp Gln Asn Phe Thr Asp Ser Lys Leu Arg Arg Ile Ile Gly Ser  
 115 120 125  
 Ile Arg Thr Leu Gly Pro Ala Asn Leu Pro Leu Ala Gln Arg Gln Gln  
 130 135 140  
 Tyr Asn Ser Leu Leu Ser Asn Met Ser Arg Ile Tyr Ser Thr Gly Lys  
 145 150 155 160  
 Val Cys Phe Pro Asn Lys Thr Ala Thr Cys Trp Ser Leu Asp Pro Glu  
 165 170 175

Leu Thr Asn Ile Leu Ala Ser Ser Arg Ser Tyr Ala Lys Leu Leu Phe  
 180 185 190  
 Ala Trp Glu Gly Trp His Asp Ala Val Gly Ile Pro Leu Lys Pro Leu  
 195 200 205  
 Tyr Gln Asp Phe Thr Ala Ile Ser Asn Glu Ala Tyr Arg Gln Asp Asp  
 210 215 220  
 Phe Ser Asp Thr Gly Ala Phe Trp Arg Ser Trp Tyr Glu Ser Pro Ser  
 225 230 235 240  
 Phe Glu Glu Ser Leu Glu His Ile Tyr His Gln Leu Glu Pro Leu Tyr  
 245 250 255  
 Leu Asn Leu His Ala Tyr Val Arg Arg Ala Leu His Arg Arg Tyr Gly  
 260 265 270  
 Asp Lys Tyr Val Asn Leu Arg Gly Pro Ile Pro Ala His Leu Leu Gly  
 275 280 285  
 Asp Met Trp Ala Gln Ser Trp Glu Asn Ile Tyr Asp Met Val Val Pro  
 290 295 300  
 Phe Pro Asp Lys Pro Asn Leu Asp Val Thr Ser Thr Met Val Gln Lys  
 305 310 315 320  
 Gly Trp Asn Ala Thr His Met Phe Arg Val Ser Glu Glu Phe Phe Thr  
 325 330 335  
 Ser Leu Gly Leu Ser Pro Met Pro Pro Glu Phe Trp Ala Glu Ser Met  
 340 345 350  
 Leu Glu Lys Pro Thr Asp Gly Arg Glu Val Val Cys His Ala Ser Ala  
 355 360 365  
 Trp Asp Phe Tyr Asn Arg Lys Asp Phe Arg Ile Lys Gln Cys Thr Arg  
 370 375 380  
 Val Thr Met Glu Gln Leu Ala Thr Val His His Glu Met Gly His Val  
 385 390 395 400  
 Gln Tyr Tyr Leu Gln Tyr Lys Asp Leu His Val Ser Leu Arg Arg Gly  
 405 410 415  
 Ala Asn Pro Gly Phe His Glu Ala Ile Gly Asp Val Leu Ala Leu Ser  
 420 425 430  
 Val Ser Thr Pro Ala His Leu His Lys Ile Gly Leu Leu Asp His Val  
 435 440 445  
 Thr Asn Asp Ile Glu Ser Asp Ile Asn Tyr Leu Leu Lys Met Ala Leu  
 450 455 460  
 Glu Lys Ile Ala Phe Leu Pro Phe Gly Tyr Leu Val Asp Gln Trp Arg  
 465 470 475 480  
 Trp Gly Val Phe Ser Gly Arg Thr Pro Pro Ser Arg Tyr Asn Phe Asp  
 485 490 495  
 Trp Trp Tyr Leu Arg Thr Lys Tyr Gln Gly Ile Cys Pro Pro Val Ala

500	505	510
Arg Asn Glu Thr His Phe Asp Ala Gly Ala Lys Phe His Ile Pro Asn 515	520	525
Val Thr Pro Tyr Ile Arg Tyr Phe Val Ser Phe Val Leu Gln Phe Gln 530	535	540
Phe His Gln Ala Leu Cys Lys Glu Ala Gly His Gln Gly Pro Leu His 545	550	555 560
Gln Cys Asp Ile Tyr Gln Ser Ala Gln Ala Gly Ala Lys Leu Lys Gln 565	570	575
Val Leu Gln Ala Gly Cys Ser Arg Pro Trp Gln Glu Val Leu Lys Asp 580	585	590
Leu Val Gly Ser Asp Ala Leu Asp Ala Lys Ala Leu Leu Glu Tyr Phe 595	600	605
Gln Pro Val Ser Gln Trp Leu Glu Glu Gln Asn Gln Arg Asn Gly Glu 610	615	620
Val Leu Gly Trp Pro Glu Asn Gln Trp Arg Pro Pro Leu Pro Asp Asn 625	630	635 640
Tyr Pro Glu Gly Ile Asp Leu Glu Thr Asp Glu Ala Lys Ala Asp Arg 645	650	655
Phe Val Glu Glu Tyr Asp Arg Thr Ala Gln Val Leu Leu Asn Glu Tyr 660	665	670
Ala Glu Ala Asn Trp Gln Tyr Asn Thr Asn Ile Thr Ile Glu Gly Ser 675	680	685
Lys Ile Leu Leu Glu Lys Ser Thr Glu Val Ser Asn His Thr Leu Lys 690	695	700
Tyr Gly Thr Arg Ala Lys Thr Phe Asp Val Ser Asn Phe Gln Asn Ser 705	710	715 720
Ser Ile Lys Arg Ile Ile Lys Lys Leu Gln Asn Leu Asp Arg Ala Val 725	730	735
Leu Pro Pro Lys Glu Leu Glu Glu Tyr Asn Gln Ile Leu Leu Asp Met 740	745	750
Glu Thr Thr Tyr Ser Leu Ser Asn Ile Cys Tyr Thr Asn Gly Thr Cys 755	760	765
Met Pro Leu Glu Pro Asp Leu Thr Asn Met Met Ala Thr Ser Arg Lys 770	775	780
Tyr Glu Glu Leu Leu Trp Ala Trp Lys Ser Trp Arg Asp Lys Val Gly 785	790	795 800
Arg Ala Ile Leu Pro Phe Phe Pro Lys Tyr Val Glu Phe Ser Asn Lys 805	810	815
Ile Ala Lys Leu Asn Gly Tyr Thr Asp Ala Gly Asp Ser Trp Arg Ser 820	825	830



Leu Tyr Glu Ser Asp Asn Leu Glu Gln Asp Leu Glu Lys Leu Tyr Gln  
 835 840 845  
 Glu Leu Gln Pro Leu Tyr Leu Asn Leu His Ala Tyr Val Arg Arg Ser  
 850 855 860  
 Leu His Arg His Tyr Gly Ser Glu Tyr Ile Asn Leu Asp Gly Pro Ile  
 865 870 875 880  
 Pro Ala His Leu Leu Gly Asn Met Trp Ala Gln Thr Trp Ser Asn Ile  
 885 890 895  
 Tyr Asp Leu Val Ala Pro Phe Pro Ser Ala Pro Asn Ile Asp Ala Thr  
 900 905 910  
 Glu Ala Met Ile Lys Gln Gly Trp Thr Pro Arg Arg Ile Phe Lys Glu  
 915 920 925  
 Ala Asp Asn Phe Phe Thr Ser Leu Gly Leu Leu Pro Val Pro Pro Glu  
 930 935 940  
 Phe Trp Asn Lys Ser Met Leu Glu Lys Pro Thr Asp Gly Arg Glu Val  
 945 950 955 960  
 Val Cys His Pro Ser Ala Trp Asp Phe Tyr Asn Gly Lys Asp Phe Arg  
 965 970 975  
 Ile Lys Gln Cys Thr Ser Val Asn Met Glu Asp Leu Val Ile Ala His  
 980 985 990  
 His Glu Met Gly His Ile Gln Tyr Phe Met Gln Tyr Lys Asp Leu Pro  
 995 1000 1005  
 Val Thr Phe Arg Glu Gly Ala Asn Pro Gly Phe His Glu Ala Ile Gly  
 1010 1015 1020  
 Asp Ile Met Ala Leu Ser Val Ser Thr Pro Lys His Leu Tyr Ser Leu  
 1025 1030 1035 1040  
 Asn Leu Leu Ser Thr Glu Gly Ser Gly Tyr Glu Tyr Asp Ile Asn Phe  
 1045 1050 1055  
 Leu Met Lys Met Ala Leu Asp Lys Ile Ala Phe Ile Pro Phe Ser Tyr  
 1060 1065 1070  
 Leu Ile Asp Gln Trp Arg Trp Arg Val Phe Asp Gly Ser Ile Thr Lys  
 1075 1080 1085  
 Glu Asn Tyr Asn Gln Glu Trp Trp Ser Leu Arg Leu Lys Tyr Gln Gly  
 1090 1095 1100  
 Leu Cys Pro Pro Val Pro Arg Ser Gln Gly Asp Phe Asp Pro Gly Ser  
 1105 1110 1115 1120  
 Lys Phe His Val Pro Ala Asn Val Pro Tyr Val Arg Tyr Phe Val Ser  
 1125 1130 1135  
 Phe Ile Ile Gln Phe Gln Phe His Glu Ala Leu Cys Arg Ala Ala Gly  
 1140 1145 1150

His Thr Gly Pro Leu His Lys Cys Asp Ile Tyr Gln Ser Lys Glu Ala  
 1155 1160 1165  
 Gly Lys Leu Leu Ala Asp Ala Met Lys Leu Gly Tyr Ser Lys Pro Trp  
 1170 1175 1180  
 Pro Glu Ala Met Lys Leu Ile Thr Gly Gln Pro Asn Met Ser Ala Ser  
 1185 1190 1195 1200  
 Ala Met Met Asn Tyr Phe Lys Pro Leu Thr Glu Trp Leu Val Thr Glu  
 1205 1210 1215  
 Asn Arg Arg His Gly Glu Thr Leu Gly Trp Pro Glu Tyr Asn Trp Ala  
 1220 1225 1230  
 Pro Asn Thr Gly Thr Thr Pro Thr Leu Pro Pro Ala Pro Ile Leu Trp  
 1235 1240 1245  
 Ile Pro Ser Val  
 1250

<210> 173  
 <211> 374  
 <212> PRT  
 <213> Mouse

<400> 173  
 Met Thr Met Thr Leu His Thr Lys Ala Ser Gly Met Ala Leu Leu His  
 1 5 10 15  
 Gln Ile Gln Gly Asn Glu Leu Glu Pro Leu Asn Arg Pro Gln Leu Lys  
 20 25 30  
 Met Pro Met Glu Arg Ala Leu Gly Glu Val Tyr Val Asp Asn Ser Lys  
 35 40 45  
 Pro Thr Val Phe Asn Tyr Pro Glu Gly Ala Ala Tyr Glu Phe Asn Ala  
 50 55 60  
 Ala Ala Ala Ala Ala Ala Ala Ser Ala Pro Val Tyr Gly Gln Ser  
 65 70 75 80  
 Gly Ile Ala Tyr Gly Pro Gly Ser Glu Ala Ala Ala Phe Ser Ala Asn  
 85 90 95  
 Ser Leu Gly Ala Phe Pro Gln Leu Asn Ser Val Ser Pro Ser Pro Leu  
 100 105 110  
 Met Leu Leu His Pro Pro Pro Gln Leu Ser Pro Phe Leu His Pro His  
 115 120 125  
 Gly Gln Gln Val Pro Tyr Tyr Leu Glu Asn Glu Pro Ser Ala Tyr Ala  
 130 135 140  
 Val Arg Asp Thr Gly Pro Pro Ala Phe Tyr Arg Ser Asn Ser Asp Asn  
 145 150 155 160  
 Arg Arg Gln Asn Gly Arg Glu Arg Leu Ser Ser Asn Glu Lys Gly  
 165 170 175

Asn Met Ile Met Glu Ser Ala Lys Glu Thr Arg Tyr Cys Ala Val Cys  
 180 185 190  
 Asn Asp Tyr Ala Ser Gly Tyr His Tyr Gly Val Trp Ser Cys Glu Gly  
 195 200 205  
 Cys Lys Ala Phe Phe Lys Arg Ser Ile Gln Gly His Asn Asp Tyr Met  
 210 215 220  
 Cys Pro Ala Thr Asn Gln Cys Thr Ile Asp Lys Asn Arg Arg Lys Ser  
 225 230 235 240  
 Cys Gln Ala Cys Arg Leu Arg Lys Cys Tyr Glu Val Gly Met Met Lys  
 245 250 255  
 Gly Gly Ile Arg Lys Asp Arg Arg Gly Gly Arg Met Leu Lys His Lys  
 260 265 270  
 Arg Gln Arg Asp Asp Leu Glu Gly Arg Asn Glu Met Gly Ala Ser Gly  
 275 280 285  
 Asp Met Arg Ala Ala Asn Leu Trp Pro Ser Pro Leu Val Ile Lys His  
 290 295 300  
 Thr Lys Lys Asn Ser Pro Ala Leu Ser Leu Thr Ala Asp Gln Met Val  
 305 310 315 320  
 Ser Ala Leu Leu Asp Ala Glu Pro Pro Met Ile Tyr Ser Glu Tyr Asp  
 325 330 335  
 Pro Ser Arg Pro Phe Ser Glu Ala Ser Met Met Gly Leu Leu Thr Asn  
 340 345 350  
 Leu Ala Asp Arg Glu Leu Val His Met Ile Asn Trp Ala Lys Arg Val  
 355 360 365  
 Pro Gly Gly Asn Ser Leu  
 370

<210> 174  
 <211> 468  
 <212> PRT  
 <213> Mouse

<400> 174  
 Met Ala Thr Leu Leu Arg Ser Lys Leu Thr Asn Val Ala Thr Ser Val  
 1 5 10 15  
 Ser Asn Lys Ser Gln Ala Lys Val Ser Gly Met Phe Ala Arg Met Gly  
 20 25 30  
 Phe Gln Ala Ala Thr Asp Glu Glu Ala Val Gly Phe Ala His Cys Asp  
 35 40 45  
 Asp Leu Asp Phe Glu His Arg Gln Gly Leu Gln Met Asp Ile Leu Lys  
 50 55 60  
 Ser Glu Gly Glu Pro Cys Gly Asp Glu Gly Ala Glu Ala Pro Val Glu  
 65 70 75 80

206

405										410					415				
Phe	Phe	Pro	Ala	Cys	Tyr	Gly	Gly	Asp	Gly	Arg	Leu	Lys	Ser	Trp	Gly				
			420					425					430						
Leu	Thr	Leu	Arg	Cys	Ala	Leu	Val	Val	Phe	Thr	Leu	Leu	Met	Ala	Ile				
		435					440					445							
Ser	Ser	Cys	Ala	Met	Tyr	Pro	Phe	Val	Glu	Leu	Tyr	Thr	Val	Arg	Val				
	450					455					460								
Val	Cys	Ser	Trp																
465																			

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
25 May 2001 (25.05.2001)

PCT

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133455 10 December 1999 (10.12.1999) IL
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- (74) Agent: REINHOLD COHN AND PARTNERS; P.O.B. 4060, 61040 Tel Aviv (IL).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- (88) Date of publication of the international search report:  
3 January 2002
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: VARIANTS OF ALTERNATIVE SPLICING

(57) Abstract: The present invention concerns novel variants, amino acid and nucleic acid sequences obtained by alternative splicing of known sequences, expression vectors and host cells containing the variants' nucleic acid sequence, and antibodies reactive with the variants' products. The invention also concerns pharmaceutical compositions containing any of the above as well as methods of detection. A preferred example is the angiotensin converting enzyme (ACE) variant.

WO 01/36632 A3

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/12 C12N15/57 C07K14/47 C07K14/705 C12N9/48  
C12Q1/68 G01N33/68 G01N33/50 A61K38/17 A61K38/48

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N A61K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EMBASE, MEDLINE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 264 948 A (MERCK & CO INC) 15 September 1993 (1993-09-15) figure 3 page 41 -page 42, line 7	2,8,9, 20-22
A	claims 9-14	1-30
X	WO 93 25677 A (GARVAN INST MED RES ;PIERCE KERRIE DIANE (AU); SELBIE LISA (AU); F) 23 December 1993 (1993-12-23)	2,8,9, 20-22
A	the whole document	1-30
	--- -/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*S\* document member of the same patent family

Date of the actual completion of the international search

30 July 2001

Date of mailing of the international search report

13.08.01

Name and mailing address of the ISA

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Authorized officer

Andres, S

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/IL 00/00766

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FURLONG T J ET AL: "MOLECULAR CHARACTERIZATION OF A HUMAN BRAIN ADENOSINE A2 RECEPTOR" MOLECULAR BRAIN RESEARCH, vol. 15, no. 1/02, 1 September 1992 (1992-09-01), pages 62-66, XP000615546 ISSN: 0169-328X the whole document ---	2,8,9
X	DATABASE EM_HUM 'Online! EMBL; Accession number : U40771; ID : HS2AAR02, 15 December 1995 (1995-12-15) "Human A2a adenosine receptor subtype (ADORA2A) gene" XP002165717 abstract ---	2
A	GELFAND M S ET AL: "ASDB: Database of alternatively spliced genes." NUCLEIC ACIDS RESEARCH, vol. 27, no. 1, 1 January 1999 (1999-01-01), pages 301-302, XP002165716 ISSN: 0305-1048 cited in the application ---	
A	CHU Y Y ET AL: "Characterization of the rat A2a adenosine receptor gene." DNA AND CELL BIOLOGY, (1996 APR) 15 (4) 329-37., XP000992998 ---	
X	BERNSTEIN K E ET AL: "THE ISOLATION OF ANGIOTENSIN-CONVERTING ENZYME CDNA" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 263, no. 23, 15 August 1988 (1988-08-15), pages 11021-11024, XP000095152 ISSN: 0021-9258 the whole document ---	2,8,9, 32,38,39
Y		1-22, 25-53, 56-61
Y	SUGIMURA K ET AL.: "Alternative splicing of the mRNA coding for the human endothelial angiotensin-converting enzyme: a new mechanism for solubilization." BIOCHEM BIOPHYS RES COMMUN 1998 JUN 18;247(2):466-72., XP002173427 the whole document ---	1-22, 25-53, 56-61

-/-



## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BERNSTEIN K E ET AL: "MOUSE ANGIOTENSIN-CONVERTING ENZYME IS A PROTEIN COMPOSED OF TWO HOMOLOGOUS DOMAINS" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 264, no. 20, 1989, pages 11945-11951, XP002173428 ISSN: 0021-9258 the whole document ---	2,8,9, 32,38,39
X	WO 90 03435 A (INST NAT SANTE RECH MED) 5 April 1990 (1990-04-05) the whole document ---	2,8-13, 32,38-44
X	WO 85 00369 A (CHIRON CORP) 31 January 1985 (1985-01-31) the whole document ---	2,8,9
X	DATABASE EM_EST 'Online! EMBL; Accession number : AI790464, 4 July 1999 (1999-07-04) MARRA, M. ET AL.: "u101e02.x1 Sugano mouse kidney mkia Mus musculus cDNA clone IMAGE:2064794 3' " XP002173429 abstract ---	2
Y	WHITE R ET AL: "STRUCTURAL ORGANIZATION AND EXPRESSION OF THE MOUSE ESTROGEN RECEPTOR" MOLECULAR ENDOCRINOLOGY, vol. 1, no. 10, 1987, pages 735-744, XP001002989 ISSN: 0888-8809 the whole document ---	1-22, 25-30
Y	LU B ET AL: "Estrogen receptor-beta mRNA variants in human and murine tissues." MOLECULAR AND CELLULAR ENDOCRINOLOGY, vol. 138, no. 1-2, 16 March 1998 (1998-03-16), pages 199-203, XP001002992 ISSN: 0303-7207 the whole document ---	1-22, 25-30
X	KOIKE S ET AL: "MOLECULAR CLONING AND CHARACTERIZATION OF RAT ESTROGEN RECEPTOR CDNA" NUCLEIC ACIDS RESEARCH, vol. 15, no. 6, 25 March 1987 (1987-03-25), pages 2499-2513, XP002026307 ISSN: 0305-1048 the whole document ---	2,8,9

-/-

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PFEFFER ULRICH ET AL: "Alternative splicing of the estrogen receptor primary transcript normally occurs in estrogen receptor positive tissues and cell lines." JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, vol. 56, no. 1-6, 1996, pages 99-105, XP001002991 ISSN: 0960-0760 the whole document	1-22, 25-30
T	WO 01 00823 A (EUROP MOLECULAR BIOLOGY LAB ;DENGHER STEFANIE (IT); FLOURIOT GILLES) 4 January 2001 (2001-01-04)	

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IL 00/00766

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2. ☒ Claims Nos.: 23 24 54 55  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
  
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
1-61 (inventions 1, 30 and 31)
  
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 23 24 54 55

Present claims 23, 24, 54 and 55 relate to compounds defined by reference to a desirable characteristic or property, namely their capacity to be an activator or deactivator of a particular protein.

The claims cover all compounds having this characteristic or property, whereas the application provides no support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for any of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search impossible. Consequently, no search has been carried out for these claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: Claims 1-30 (all partially)

A nucleic acid sequence defined by SEQ ID 1 and its corresponding aminoacid sequence SEQ ID 88. An antibody binding specifically to the protein, vectors and hosts expressing the nucleic acid, pharmaceutical compositions containing them and their uses in therapy or diagnostic.

2. Claims: Invention 2: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 2 and 89.

3. Claims: Invention 3: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 3 and 90.

4. Claims: Invention 4: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 4,5,91 and 92.

5. Claims: Invention 5: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 6 and 93.

6. Claims: Invention 6: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 7 and 94.

7. Claims: Invention 7: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 8 and 95.

8. Claims: Invention 8: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 9,10,96 and 97.

9. Claims: Invention 9: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 11 and 98.

10. Claims: Invention 10: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 12 and 99.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

11. Claims: Invention 11: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 13-16 and 100-103.
12. Claims: Invention 12: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 17-19, 104-106 and 163.
13. Claims: Invention 13: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 20, 107 and 159.
14. Claims: Invention 14: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 21-24, 61, 62, 108-111, 149, 150 and 160-162.
15. Claims: Invention 15: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 25 and 112.
16. Claims: Invention 16: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 26, 27, 113 and 114.
17. Claims: Invention 17: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 28, 64, 115, 152 and 164.
18. Claims: Invention 18: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 29, 116 and 139.
19. Claims: Invention 19: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 30-34, 52-55, 117-121 and 140-143.
20. Claims: Invention 20: Claims 1-30 (all partially)  
As for subject 1, but concerning SEQ IDs 35, 122, 170 and 171.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

21. Claims: Invention 21: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 36 and 123.

22. Claims: Invention 22: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 37,38,124,125 and 167.

23. Claims: Invention 23: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 39 and 126.

24. Claims: Invention 24: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 40,45,46,127, 132,133 and 168.

25. Claims: Invention 25: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 41 and 128.

26. Claims: Invention 26: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 42,43,48-50, 129,130 and 135-137.

27. Claims: Invention 27: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 44 and 131.

28. Claims: Invention 28: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 47 and 134.

29. Claims: Invention 29: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 51,138 and 165.

30. Claims: Invention 30: Claims 1-30 (all partially) and  
claims 31-61

As for subject 1, but concerning SEQ IDs 56,85,144 and 172.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

31. Claims: Invention 31: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 57,145 and 173.

32. Claims: Invention 32: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 58 and 146.

33. Claims: Invention 33: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 59 and 147.

34. Claims: Invention 34: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 60,148 and 174.

35. Claims: Invention 35: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 63 and 151.

36. Claims: Invention 36: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 65 and 153.

37. Claims: Invention 37: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 66 and 154.

38. Claims: Invention 38: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 67 and 155.

39. Claims: Invention 39: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 68,69,156,157 and 166.

40. Claims: Invention 40: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 70,158 and 169.

41. Claims: Inventions 41 to 56: Claims 1-30 (all partially)

As for subject 1, but concerning SEQ IDs 71-84, 86 and 87



FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

respectively.

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